

10/ 023,099

NEWS 45 Jun 25 HSDB has been reloaded

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 13:07:12 ON 01 JUL 2003

=> file reg	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:07:21 ON 01 JUL 2003
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 30 JUN 2003 HIGHEST RN 540462-79-1
DICTIONARY FILE UPDATES: 30 JUN 2003 HIGHEST RN 540462-79-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>
Uploading 10023099.str

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

Welcome to STN International! Enter x:x

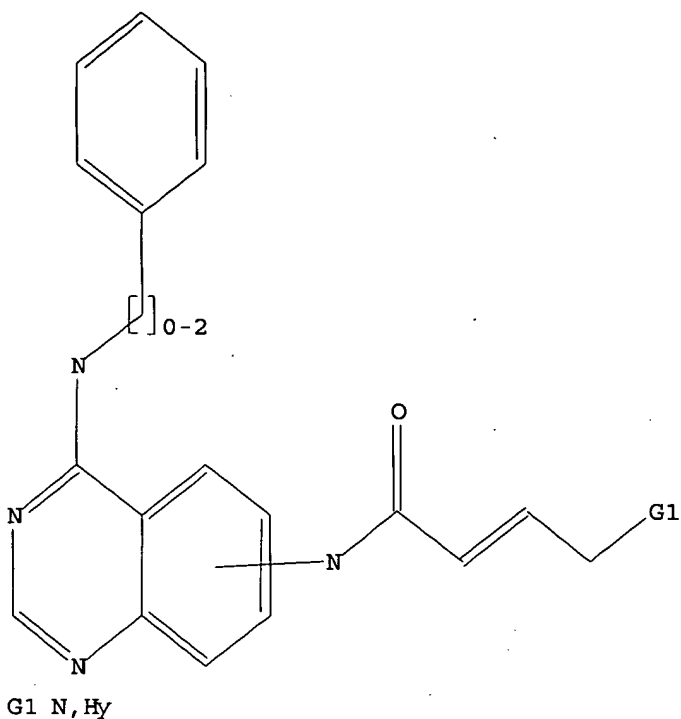
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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	Jun 03	New e-mail delivery for search results now available
NEWS	4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	7	Sep 03	JAPIO has been reloaded and enhanced
NEWS	8	Sep 16	Experimental properties added to the REGISTRY file
NEWS	9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS	10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS	11	Oct 24	BEILSTEIN adds new search fields
NEWS	12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS	13	Nov 18	DKILIT has been renamed APOLLIT
NEWS	14	Nov 25	More calculated properties added to REGISTRY
NEWS	15	Dec 04	CSA files on STN
NEWS	16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS	17	Dec 17	TOXCENTER enhanced with additional content
NEWS	18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS	19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS	20	Feb 13	CANCERLIT is no longer being updated
NEWS	21	Feb 24	METADEx enhancements
NEWS	22	Feb 24	PCTGEN now available on STN
NEWS	23	Feb 24	TEMA now available on STN
NEWS	24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS	25	Feb 26	PCTFULL now contains images
NEWS	26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS	27	Mar 20	EVENTLINE will be removed from STN
NEWS	28	Mar 24	PATDPAFULL now available on STN
NEWS	29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS	30	Apr 11	Display formats in DGENE enhanced
NEWS	31	Apr 14	MEDLINE Reload
NEWS	32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS	33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS	34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS	35	Apr 28	RDISCLOSURE now available on STN
NEWS	36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS	37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS	38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS	39	May 16	CHEMREACT will be removed from STN
NEWS	40	May 19	Simultaneous left and right truncation added to WSCA
NEWS	41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS	42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS	43	Jun 06	PASCAL enhanced with additional data
NEWS	44	Jun 20	2003 edition of the FSTA Thesaurus is now available



Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful
 FULL SEARCH INITIATED 13:07:44 FILE 'REGISTRY'
 FULL SCREEN SEARCH COMPLETED - 792 TO ITERATE

100.0% PROCESSED 792 ITERATIONS 306 ANSWERS
 SEARCH TIME: 00.00.01

L2 306 SEA SSS FUL L1

=> file caplus		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	148.15	148.36

FILE 'CAPLUS' ENTERED AT 13:07:58 ON 01 JUL 2003
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FILE LAST UPDATED: 30 Jun 2003 (20030630/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 12

L3 13 L2

=> d 13 1- ibib abs hitstr

YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:487536 CAPLUS

DOCUMENT NUMBER: 137:63250

TITLE: Quinazoline derivatives as inhibitors of human EFG tyrosine kinase

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Blech, Stefan; Jung, Birgit; Baum, Elke; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

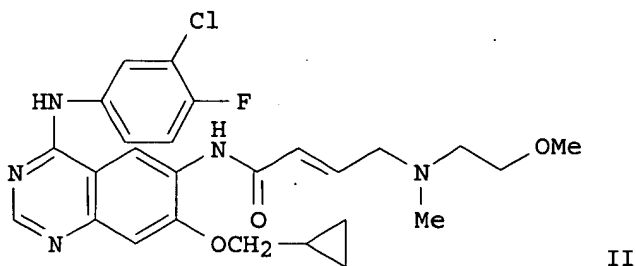
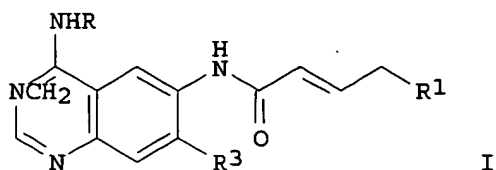
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050043	A1	20020627	WO 2001-EP14569	20011212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10063435	A1	20020704	DE 2000-10063435	20001220
AU 2002019174	A5	20020701	AU 2002-19174	20011212
US 2002173509	A1	20021121	US 2001-23099	20011217
PRIORITY APPLN. INFO.:			DE 2000-10063435 A	20001220
			US 2000-259201P P	20001228
			WO 2001-EP14569 W	20011212

OTHER SOURCE(S): MARPAT 137:63250

GI

Pregnant Version



AB Quinazoline derivs. I [R = PhCH₂, PhCHMe, 3,4-Cl(F)C₆H₃; R₁ = NMeR₂, NEt₂, NEtCH₂CH₂OMe, N(CH₂CH₂OMe)₂, morpholino; R₂ = Me, Et, CHMe₂, cyclopropyl, CH₂CH₂OMe, 3-tetrahydrofuryl, 2-tetrahydrofurylmethyl, 3-tetrahydrofurylmethyl, 4-tetrahydropyranyl, 4-tetrahydropyranylmethyl; R₃ = cyclopropylmethoxy, cyclobutyloxy, cyclopentyloxy, 3-tetrahydrofuranlyloxy, 2-tetrahydrofuranlylmethoxy, 3-tetrahydrofuranlylmethoxy, 4-tetrahydropyranyloxy, 4-tetrahydropyranylmethoxy] were prepd. for use as inhibitors of signal transduction caused by human EFG receptor tyrosine kinase. They are useful in the treatment of tumoral diseases, diseases of the lung and the respiratory tract, the gastrointestinal tract, and the gallbladder and bile ducts. Thus, the quinazoline II was prepd. by converting bromocrotonic acid to its chloride, and reaction with 4-[(3-chloro-4-fluorophenyl)amino]-6-amino-7-cyclopropylmethoxyquinazoline, followed by MeNHCH₂CH₂OMe. II had an IC₅₀ against human EFG receptor kinase of 0.7 nM.

IT 439081-10-4P 439081-11-5P 439081-13-7P
439081-18-2P 439081-30-8P 439081-40-0P
439081-41-1P 439081-42-2P 439081-48-8P

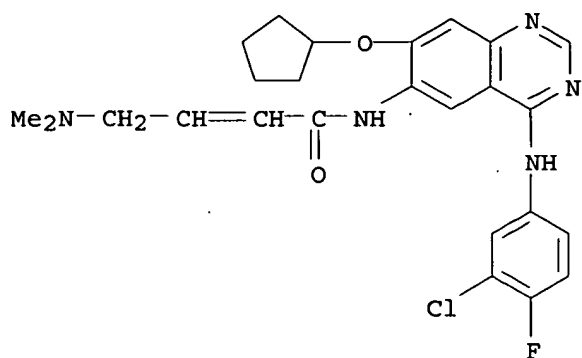
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

RN 439081-10-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

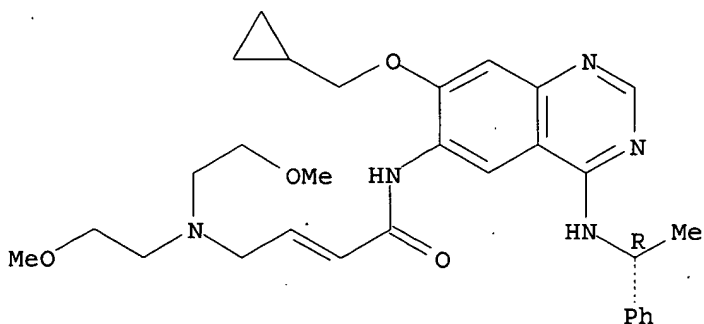
10/ 023,099



RN 439081-11-5 CAPLUS

CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[7-(cyclopropylmethoxy)-4-[[1R]-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

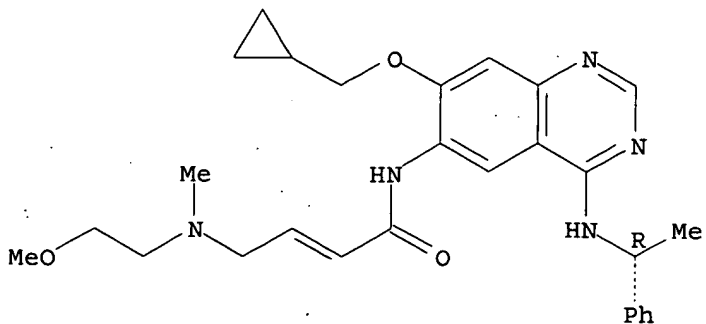
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-13-7 CAPLUS

CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[1R]-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



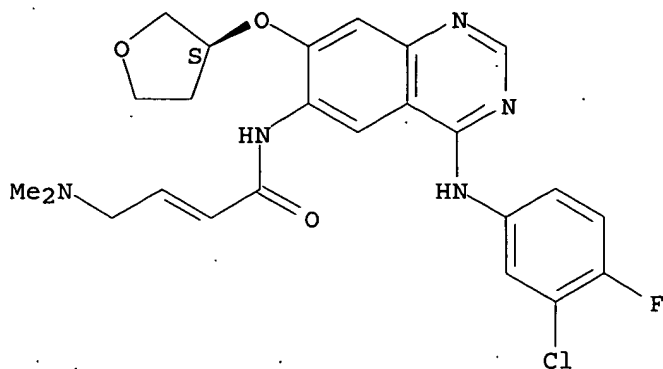
RN 439081-18-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

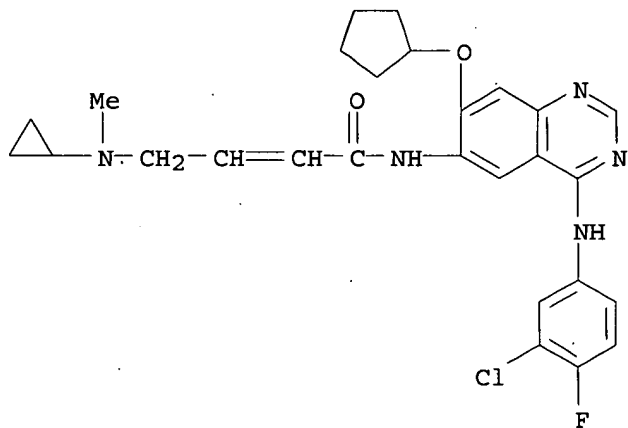
10/ 023,099

Double bond geometry unknown.



RN 439081-30-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)

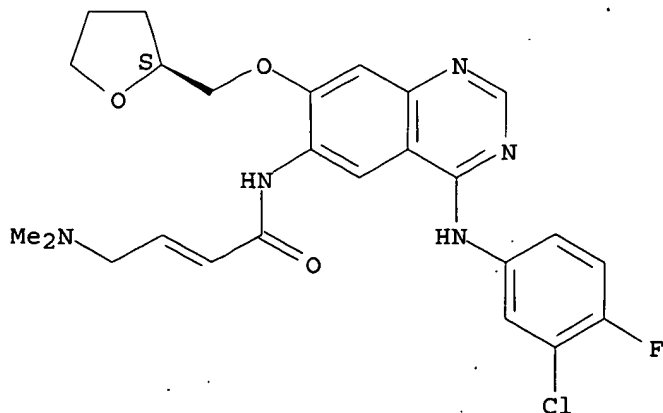


RN 439081-40-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[2-(cyclopentylmethoxy)]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



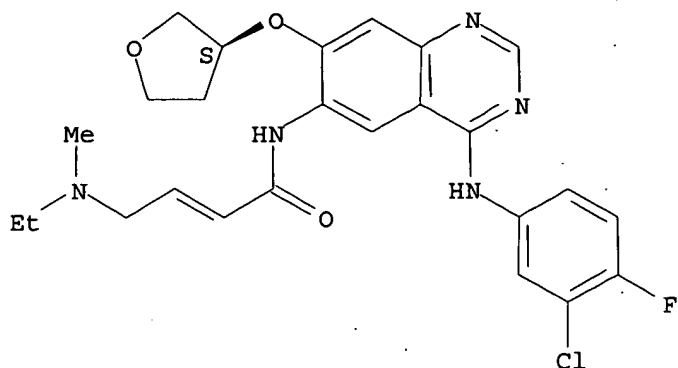
10/ 023,099

RN 439081-41-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(ethylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

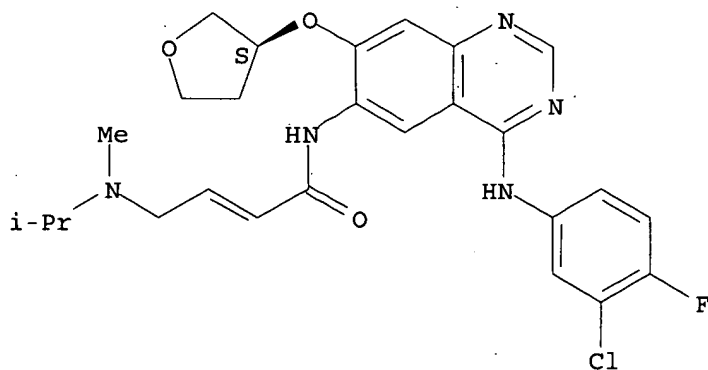


RN 439081-42-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

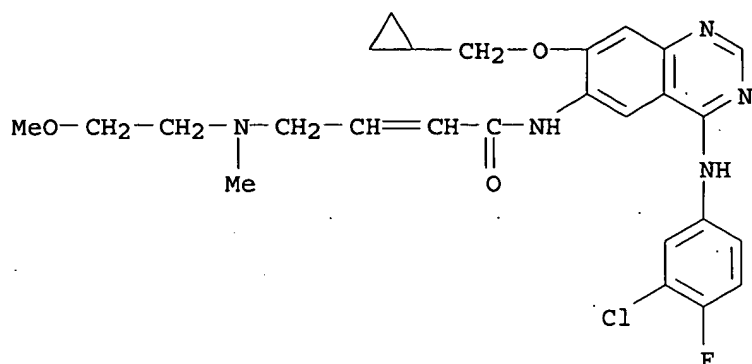
Absolute stereochemistry.

Double bond geometry unknown.



RN 439081-48-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

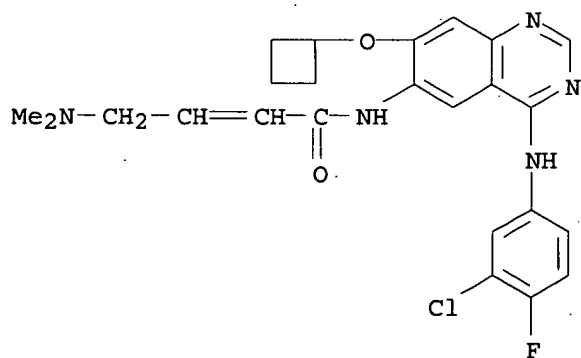


IT 439081-09-1P 439081-12-6P 439081-14-8P
 439081-15-9P 439081-16-0P 439081-17-1P
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 439081-22-8P 439081-23-9P 439081-24-0P
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 439081-38-6P 439081-39-7P 439081-43-3P
 439081-44-4P 439081-45-5P 439081-46-6P
 439081-47-7P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

RN 439081-09-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



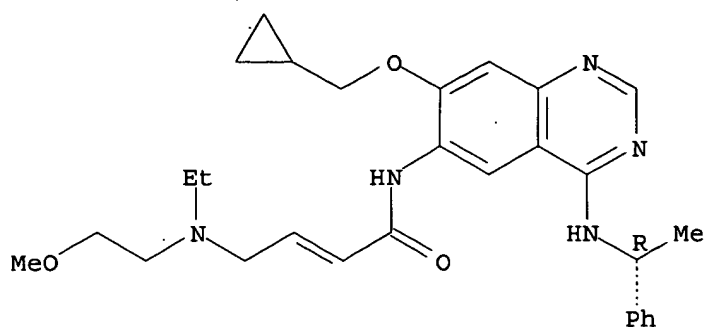
RN 439081-12-6 CAPLUS

CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[ethyl (2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

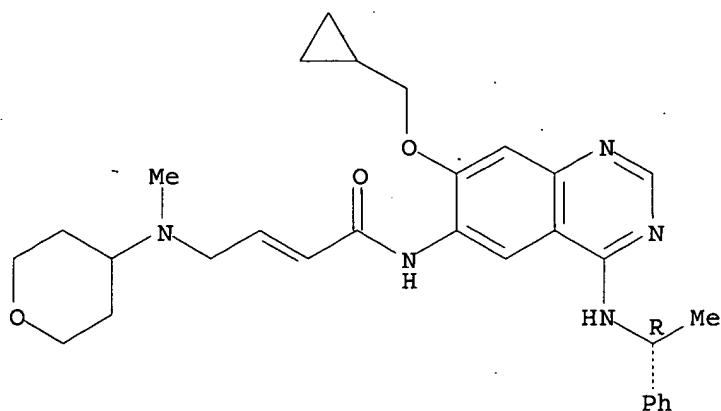
10/ 023,099



RN 439081-14-8 CAPLUS

CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

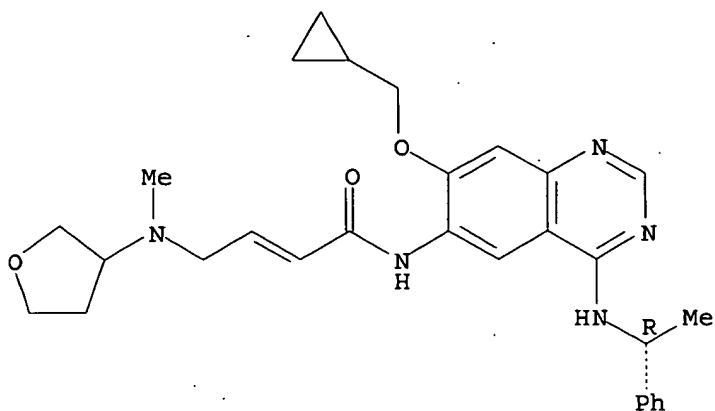
Absolute stereochemistry.
Double bond geometry unknown.



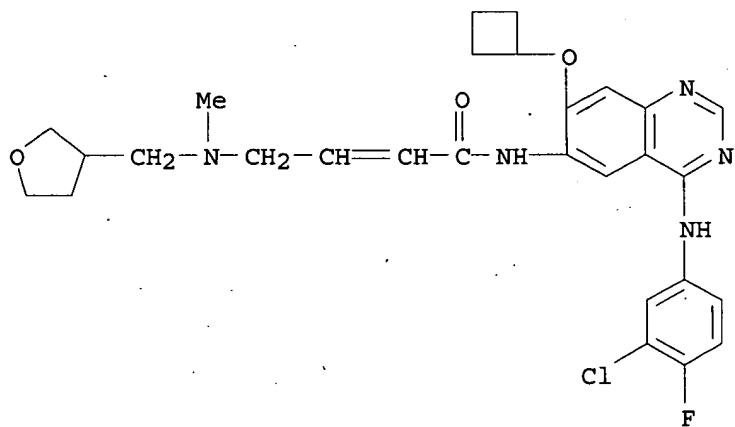
RN 439081-15-9 CAPLUS

CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-3-furanyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

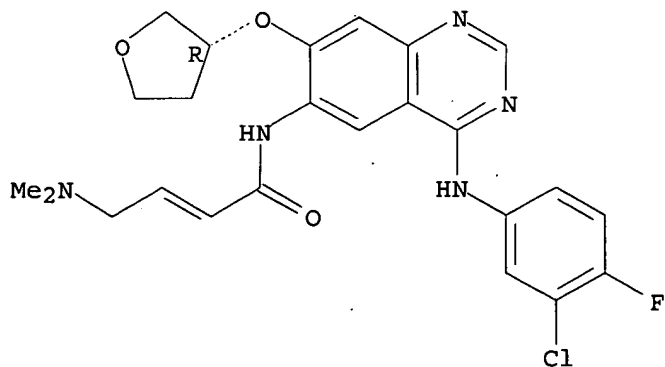


RN 439081-16-0 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-3-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 439081-17-1 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

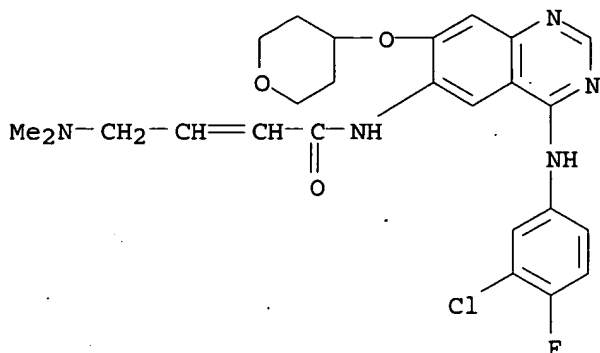
Absolute stereochemistry.
 Double bond geometry unknown.



10/ 023,099

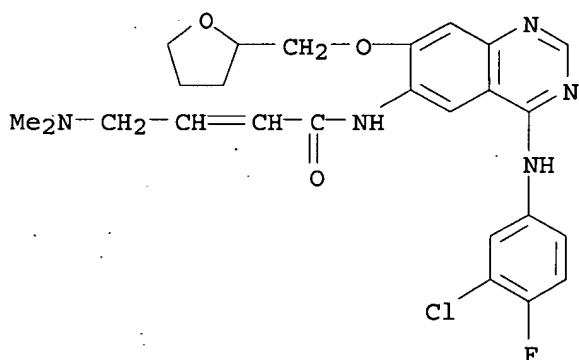
RN 439081-19-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



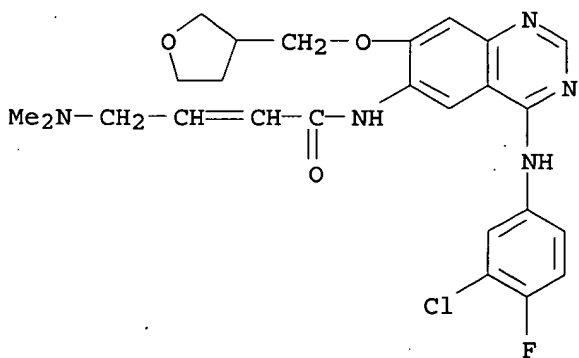
RN 439081-20-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 439081-21-7 CAPLUS

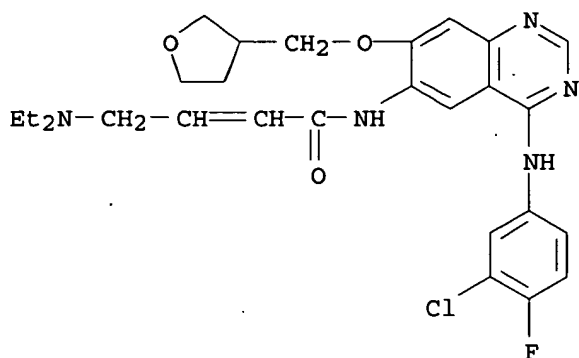
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 439081-22-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

10/ 023,099

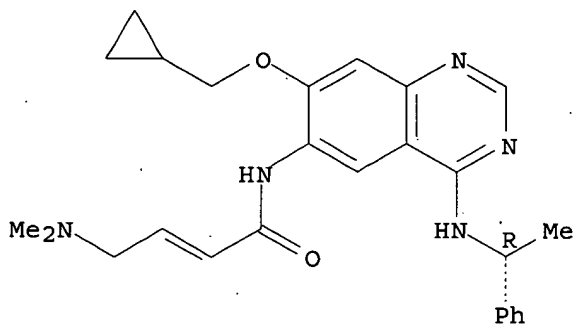


RN 439081-23-9 CAPLUS

CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

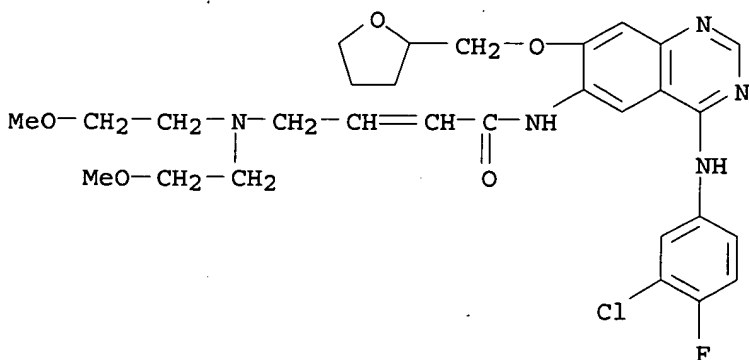
Absolute stereochemistry.

Double bond geometry unknown.



RN 439081-24-0 CAPLUS

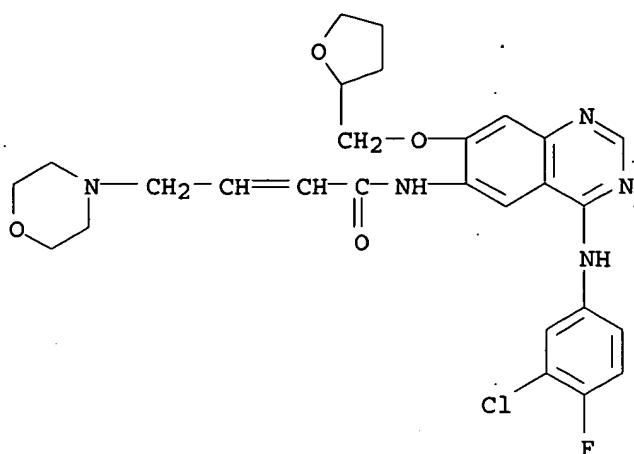
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 439081-25-1 CAPLUS

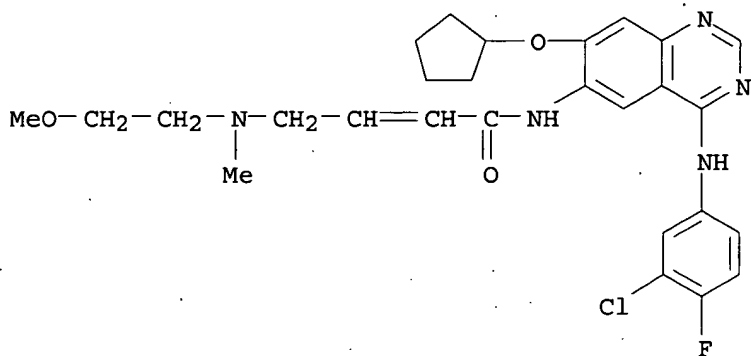
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

10/ 023,099



RN 439081-26-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

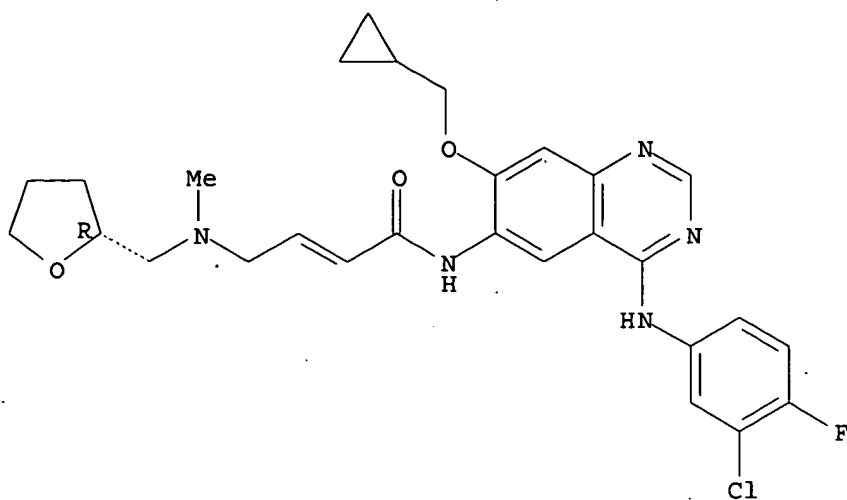


RN 439081-27-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(2R)-tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

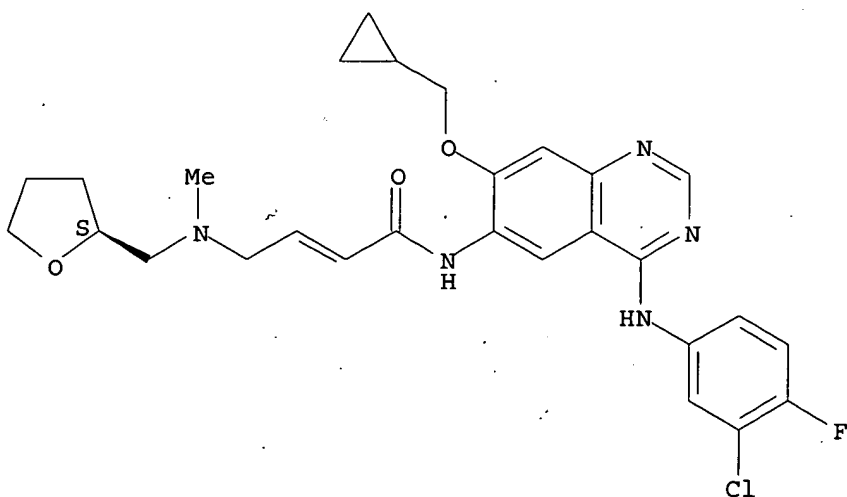
10/ 023,099



RN 439081-28-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(2S)-tetrahydro-2-furanyl]methyl]amino]- (9CI)
(CA INDEX NAME)

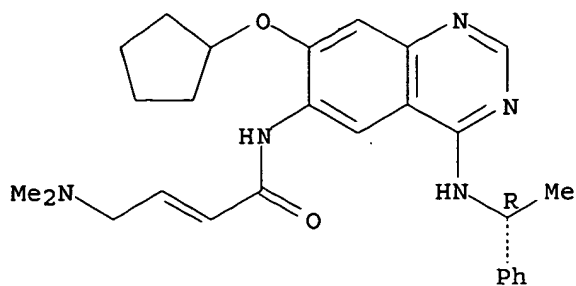
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Double bond geometry unknown.



RN 439081-29-5 CAPLUS

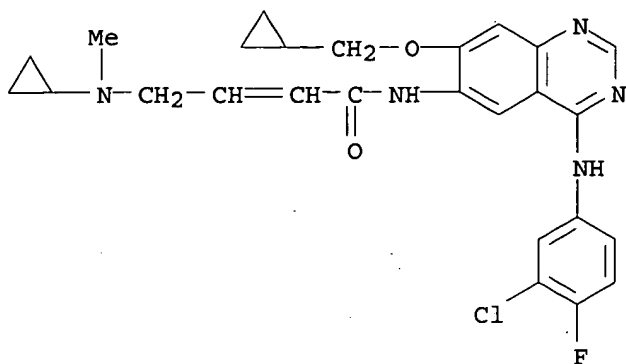
CN 2-Butenamide, N-[7-(cyclopentyloxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



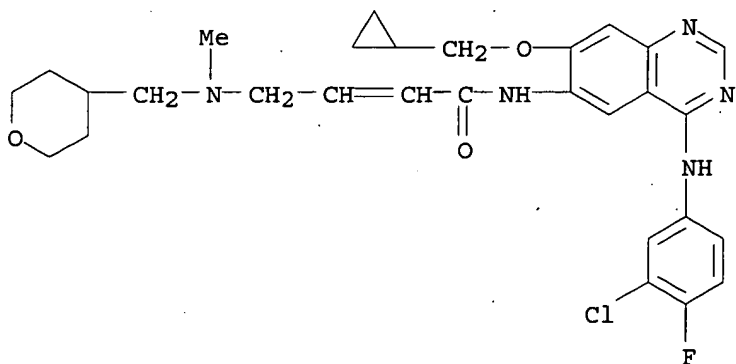
RN 439081-31-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)



RN 439081-32-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-2H-pyran-4-yl)methyl]amino]- (9CI) (CA INDEX NAME)

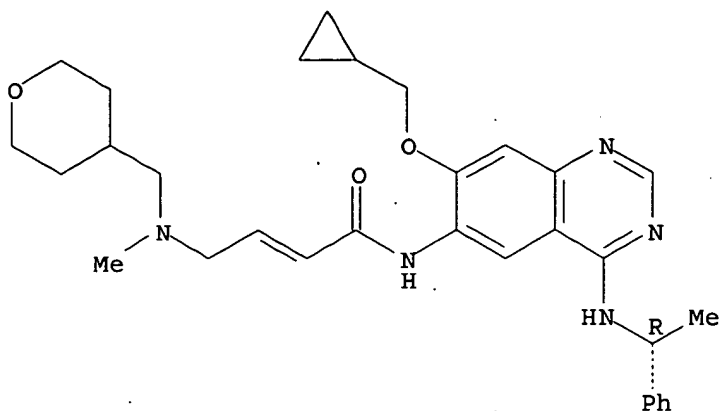


RN 439081-33-1 CAPLUS

CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl[(tetrahydro-2H-pyran-4-yl)methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

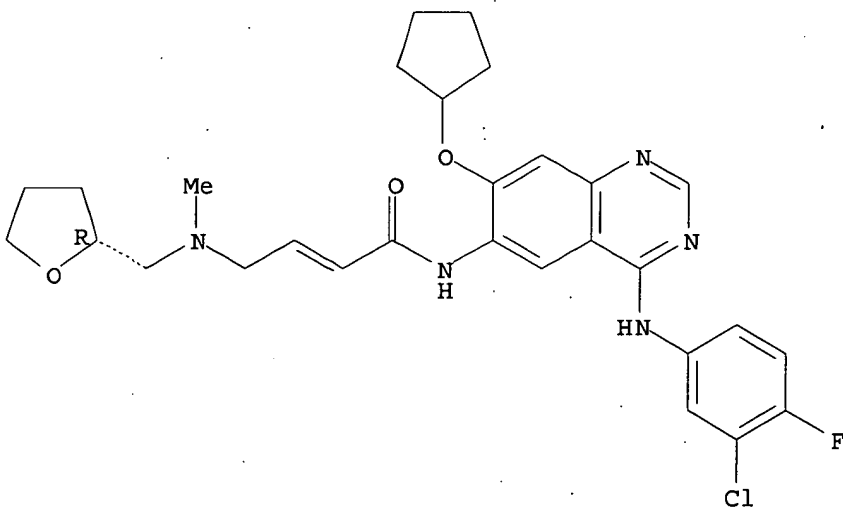
10/ 023,099



RN 439081-34-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl[(2R)-tetrahydro-2-furanyl)methyl]amino]- (9CI)
(CA INDEX NAME)

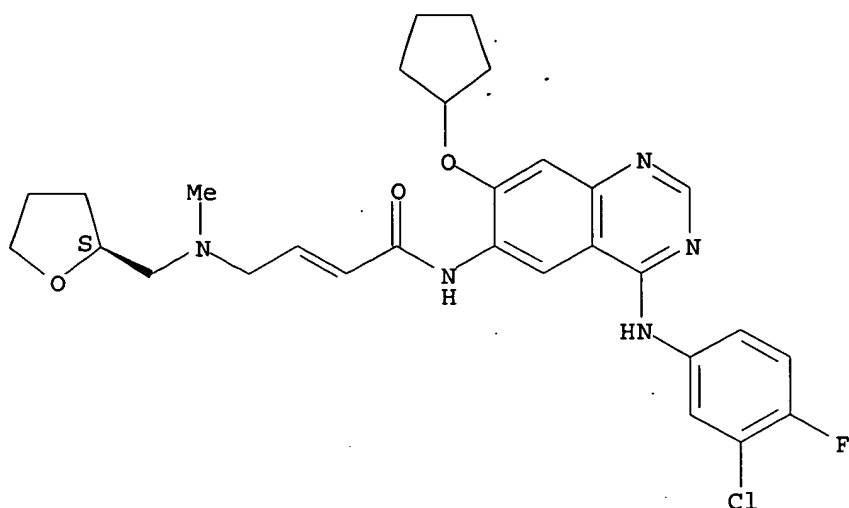
Absolute stereochemistry.
Double bond geometry unknown.



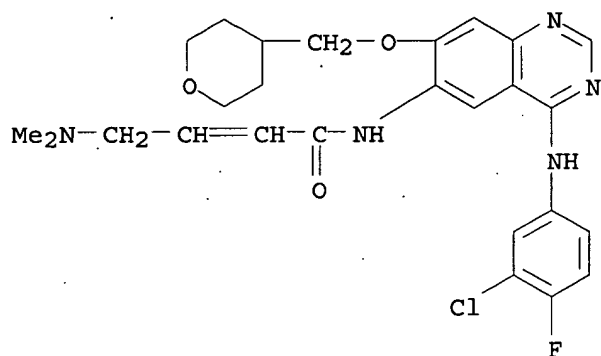
RN 439081-35-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl[(2S)-tetrahydro-2-furanyl)methyl]amino]- (9CI)
(CA INDEX NAME)

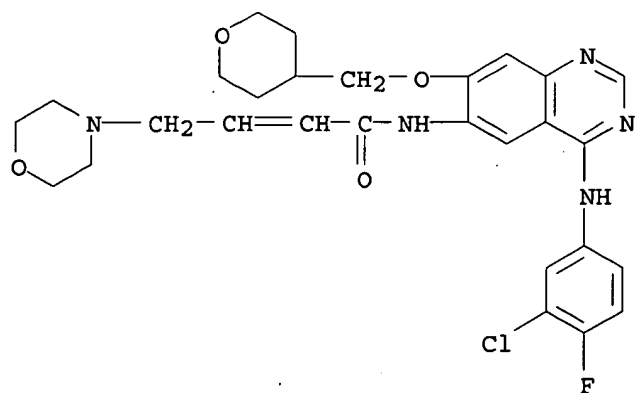
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-36-4 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-(dimethylamino)-(9CI) (CA INDEX NAME)



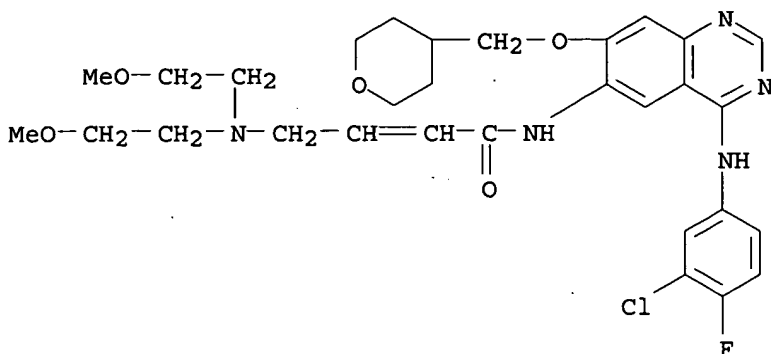
RN 439081-37-5 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-(4-morpholinyl)-(9CI) (CA INDEX NAME)



10/ 023,099

RN 439081-38-6 CAPLUS

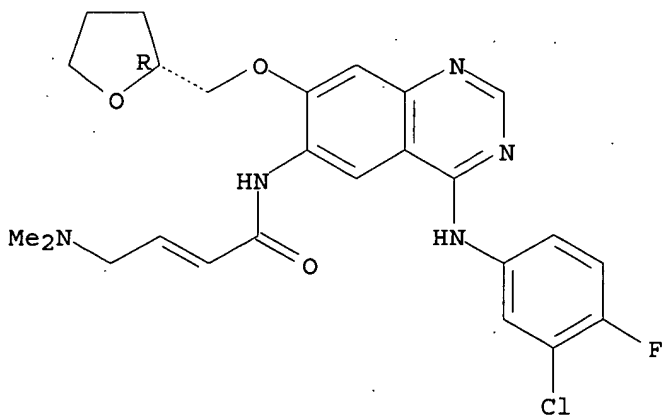
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 439081-39-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

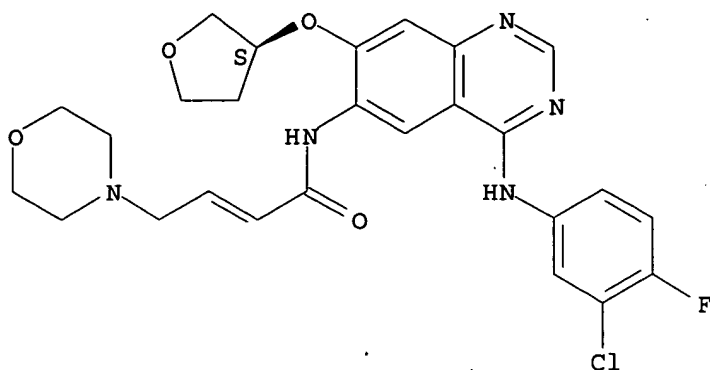
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-43-3 CAPLUS

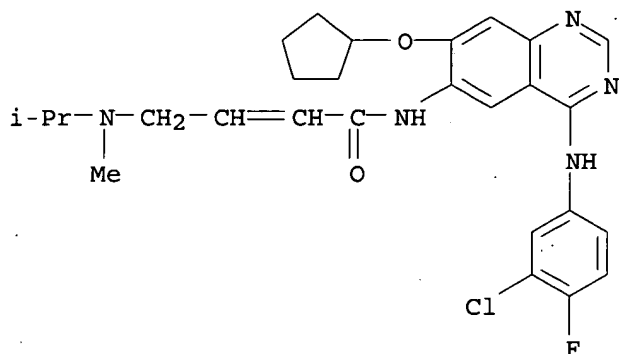
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-44-4 CAPLUS

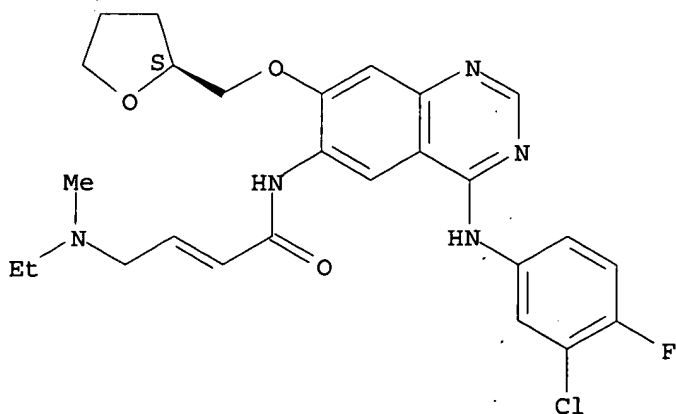
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]-(9CI) (CA INDEX NAME)



RN 439081-45-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[2S]-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(ethylmethylamino)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



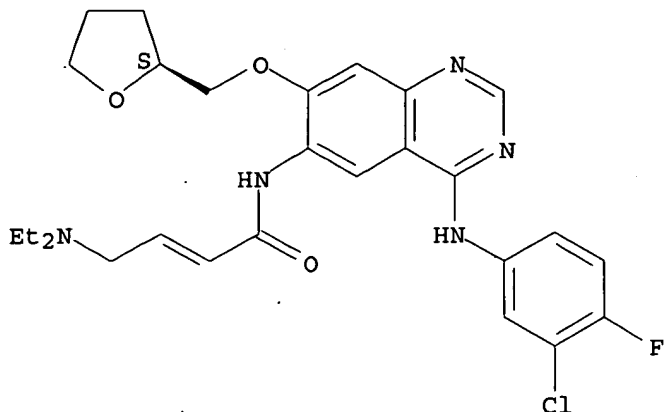
RN 439081-46-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[2S]-tetrahydro-2-

10/ 023,099

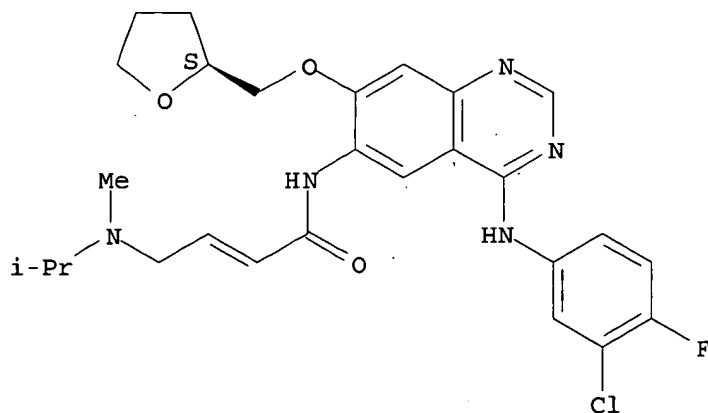
furanyl]methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-47-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[2-(2-furanyl)ethoxy]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:171892 CAPLUS
DOCUMENT NUMBER: 136:216762
TITLE: Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

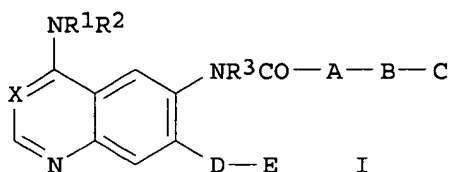
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018376	A1	20020307	WO 2001-EP9536	20010818
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10042062	A1	20020307	DE 2000-10042062	20000826
AU 2001095482	A5	20020313	AU 2001-95482	20010818
EP 1315720	A1	20030604	EP 2001-976108	20010818
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2002115675	A1	20020822	US 2001-934631	20010822
PRIORITY APPLN. INFO.:			DE 2000-10042062 A	20000826
			US 2000-230542P P	20000905
			WO 2001-EP9536 W	20010818

OTHER SOURCE(S): MARPAT 136:216762

GI



AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 = (substituted) Ph, PhCH2, 1-phenylethyl; R3 = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = (substituted) alkenyl, alkenylcarbonyl, etc.; C = (substituted) 2-oxomorpholin-4-yl, etc; D = oxyalkenyl, O; E = (substituted) amino, alkenylimino, imidazolyl, cycloalkyl; or DE = H, (substituted) alkoxy, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(ethoxycarbonylmethyl)-N-((R)-2-hydroxy-3-methoxypropyl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and MeSO2OH in MeCN were stirred for 4 h under reflux to give 69% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[(R)-2-methoxymethyl-6-oxomorpholin-4-yl]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 2 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT 402569-98-6P 402569-99-7P 402570-00-7P
402570-01-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

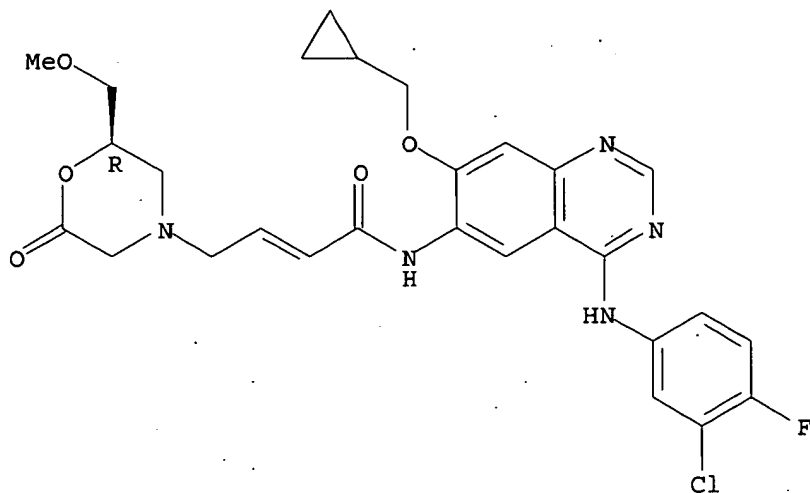
(prepn. of (amino) (heterocyclylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402569-98-6 CAPLUS

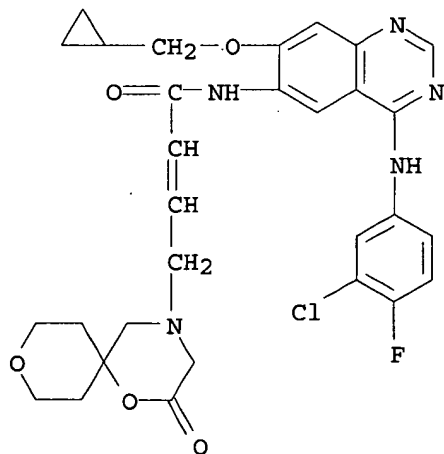
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

10/ 023,099

Absolute stereochemistry.
Double bond geometry unknown.

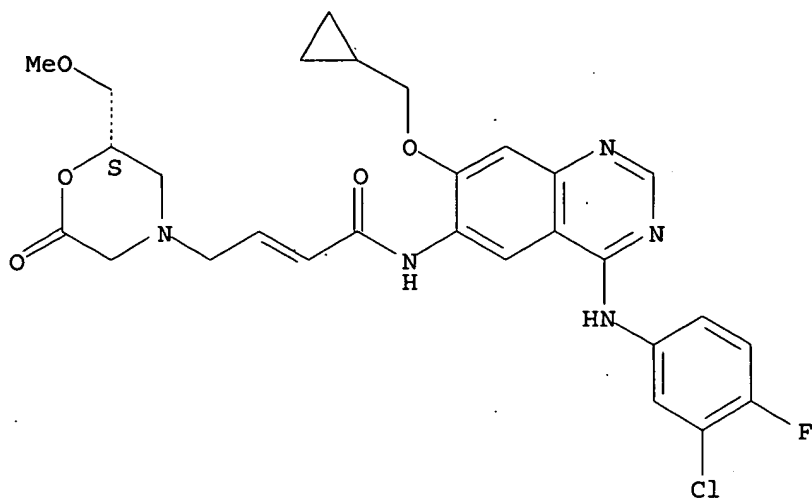


RN 402569-99-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-1,9-dioxaspiro[5.5]undec-4-yl)- (9CI) (CA INDEX NAME)

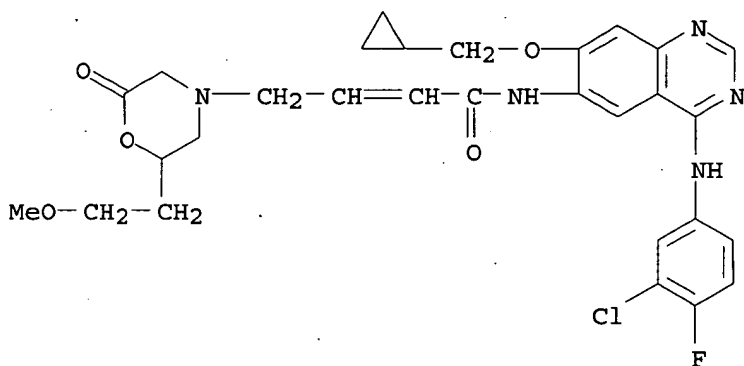


RN 402570-00-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



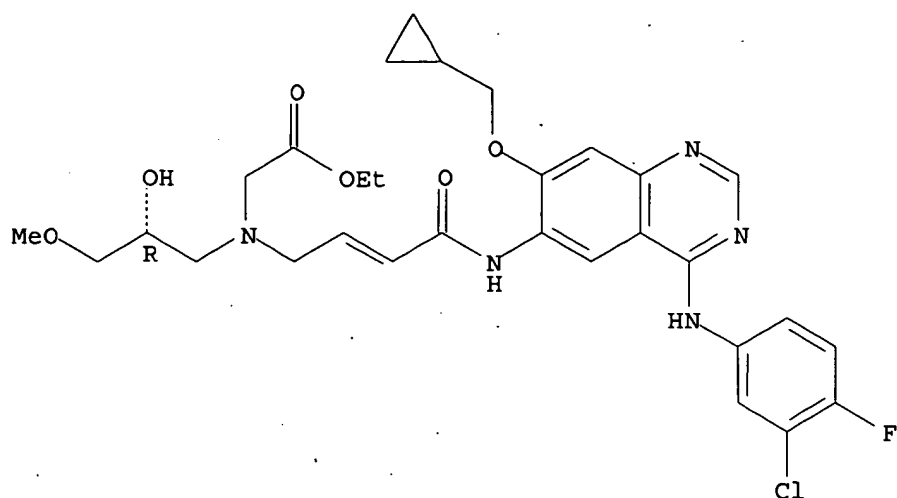
RN 402570-01-8 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[2-(2-methoxyethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)



IT 402569-87-3P 402569-89-5P 402569-90-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of (amino)(heterocyclylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)
 RN 402569-87-3 CAPLUS
 CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

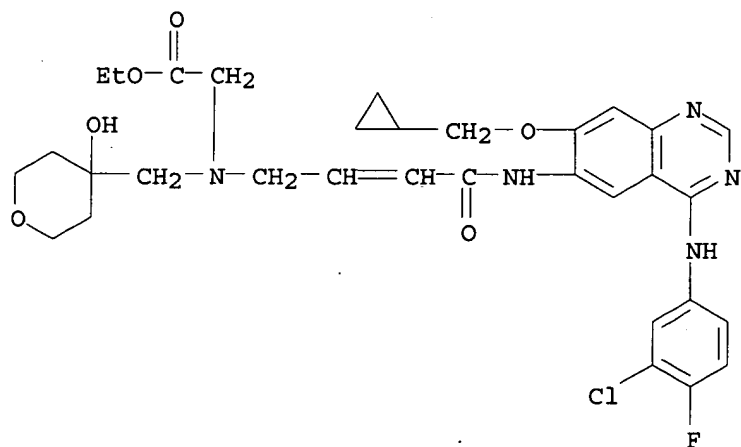
Absolute stereochemistry.
 Double bond geometry unknown.

10/ 023,099



RN 402569-89-5 CAPLUS

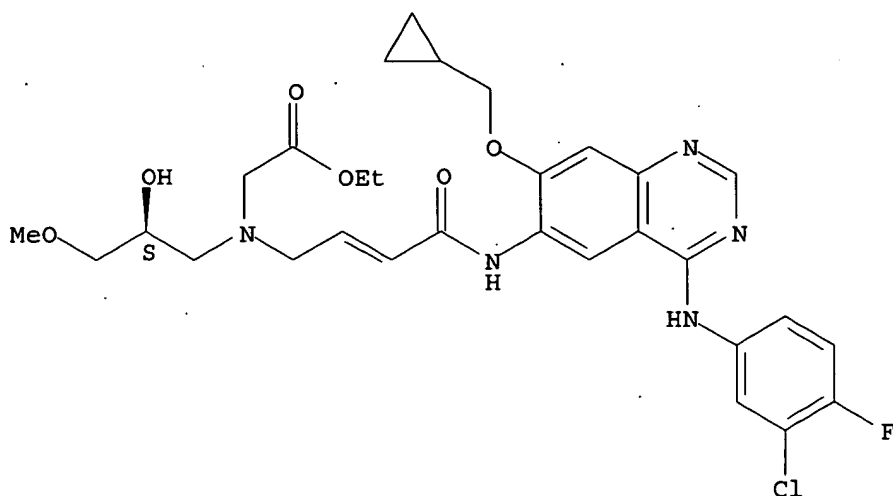
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxy-3-methoxypropyl]methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 402569-90-8 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxy-3-methoxypropyl]methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:171889 CAPLUS

DOCUMENT NUMBER: 136:232315

TITLE: Preparation of 4-amino-6-vinylcarbonylaminoquinazoline
s as epidermal growth factor receptor signal
transduction inhibitors

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit;
Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

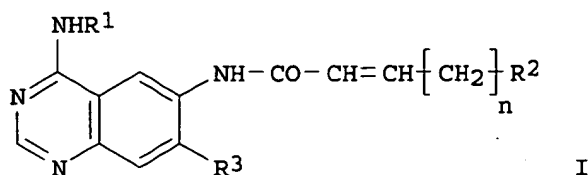
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018373	A1	20020307	WO 2001-EP9537	20010818
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10042060	A1	20020307	DE 2000-10042060	20000826
US 2002077330	A1	20020620	US 2001-929931	20010815
AU 2001084021	A5	20020313	AU 2001-84021	20010818
EP 1315717	A1	20030604	EP 2001-962953	20010818
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRIORITY APPLN. INFO.:			DE 2000-10042060 A	20000826
			US 2000-230389P P	20000906
			WO 2001-EP9537 W	20010818

OTHER SOURCE(S): MARPAT 136:232315

GI



AB Title compds. [I; R1 = PhCH₂, 1-phenylethyl, (substituted) Ph; R2 = N-[(1,3-dioxolan-2-yl)methyl]methylamino, (substituted) R₄OCOCH₂NCH₂CH₂OH, 2-oxomorpholin-4-yl; R₄ = H, alkyl; R₃ = H, (alkoxy)alkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; n = 1-3], were prepd. Thus, a mixt. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and diisopropylethylamine in THF was dropwise treated under ice-cooling with BrCH₂CH:CHCO₂Cl (prepn. given) in CH₂Cl₂ followed by stirring for 1 h under ice-cooling and for 2 h at room temp. and addn. of (S)-(2-hydroxypropylamino)acetic acid tert-Bu ester in CH₂Cl₂ to give after stirring over night at room temp. and stirring for 5 h at 60.degree. 64% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(tert-butyloxycarbonylmethyl)-N-((S)-2-hydroxyprop-1-yl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC₅₀ = 0.02-15 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT 402855-15-6P 402855-53-2P

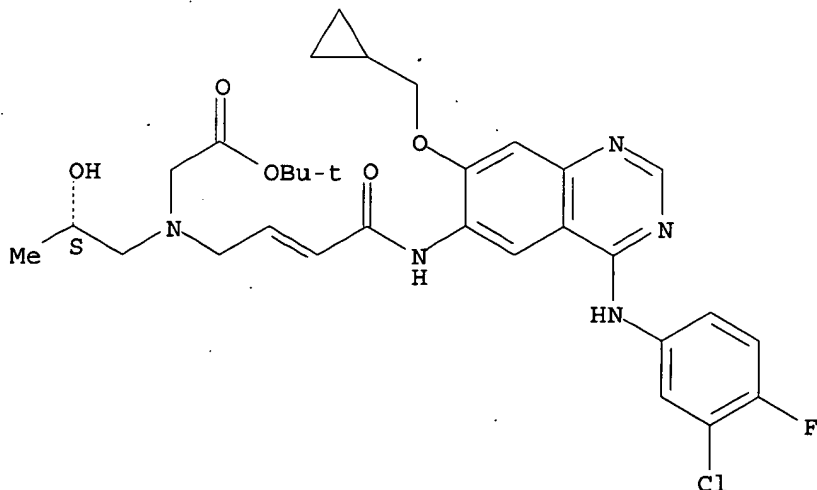
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402855-15-6 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



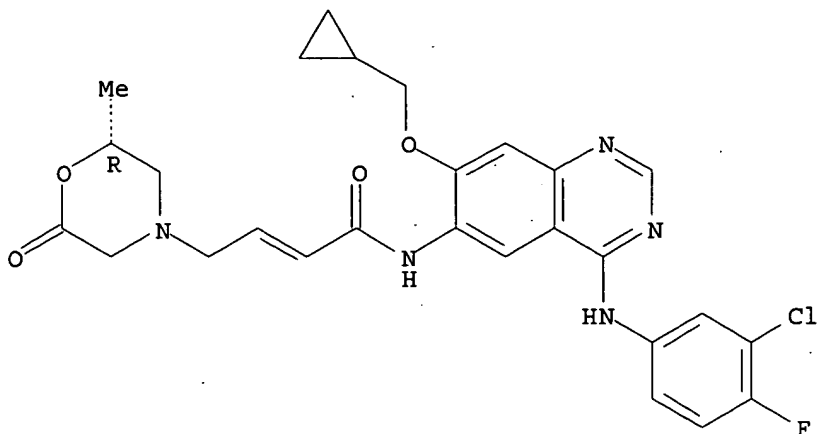
10/ 023,099

RN 402855-53-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



IT 402855-16-7P 402855-17-8P 402855-18-9P
402855-19-0P 402855-20-3P 402855-21-4P
402855-22-5P 402855-23-6P 402855-24-7P
402855-25-8P 402855-26-9P 402855-27-0P
402855-28-1P 402855-29-2P 402855-30-5P
402855-31-6P 402855-32-7P 402855-33-8P
402855-34-9P 402855-35-0P 402855-36-1P
402855-37-2P 402855-38-3P 402855-39-4P
402855-40-7P 402855-41-8P 402855-42-9P
402855-43-0P 402855-44-1P 402855-45-2P
402855-46-3P 402855-47-4P 402855-48-5P
402855-49-6P 402855-50-9P 402855-51-0P
402855-52-1P 402855-54-3P 402855-55-4P
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402855-74-7P 402855-75-8P 402855-76-9P
402855-77-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

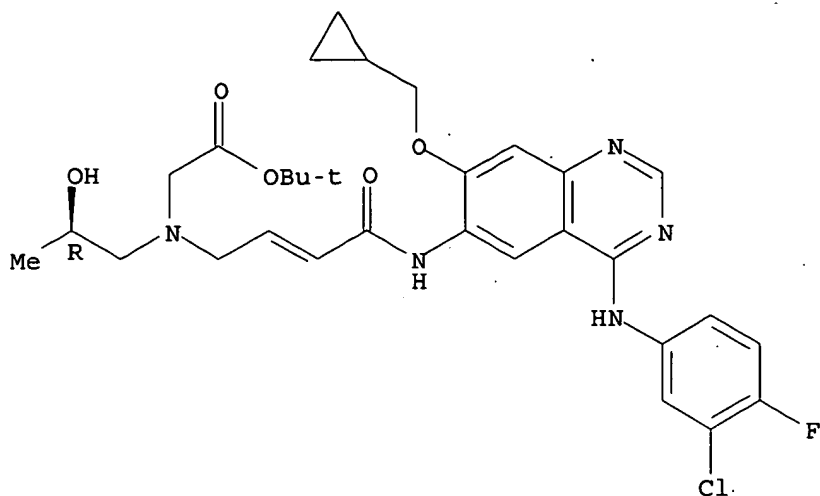
RN 402855-16-7 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

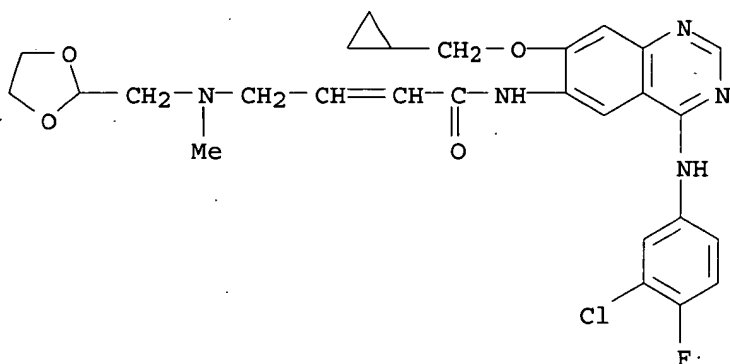
Double bond geometry unknown.

10/ 023,099



RN 402855-17-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(1,3-dioxolan-2-ylmethyl)methylamino]- (9CI) (CA INDEX NAME)

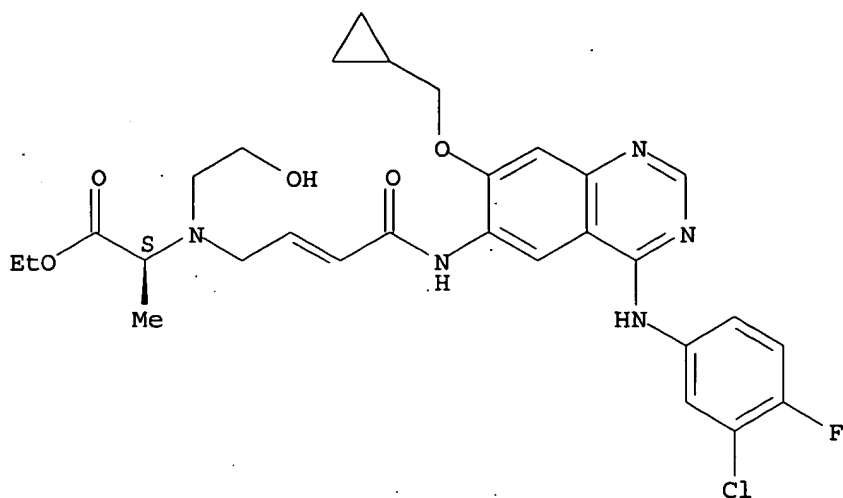


RN 402855-18-9 CAPLUS

CN L-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

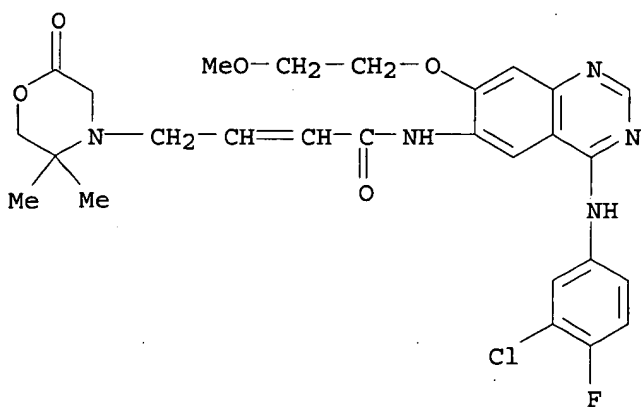
Absolute stereochemistry.
Double bond geometry unknown.

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RN 402855-19-0 CAPLUS

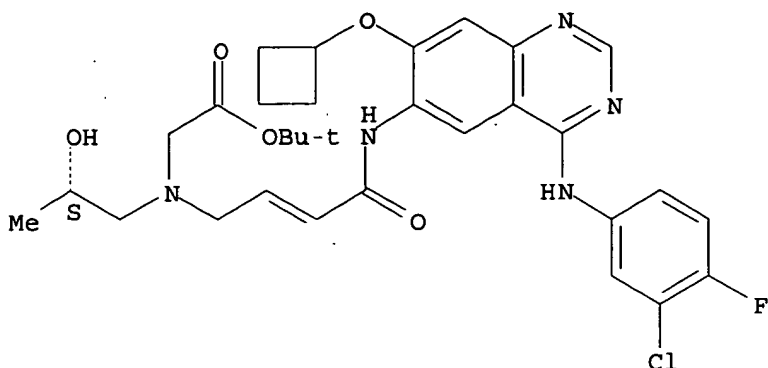
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(2-methoxyethoxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)



RN 402855-20-3 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

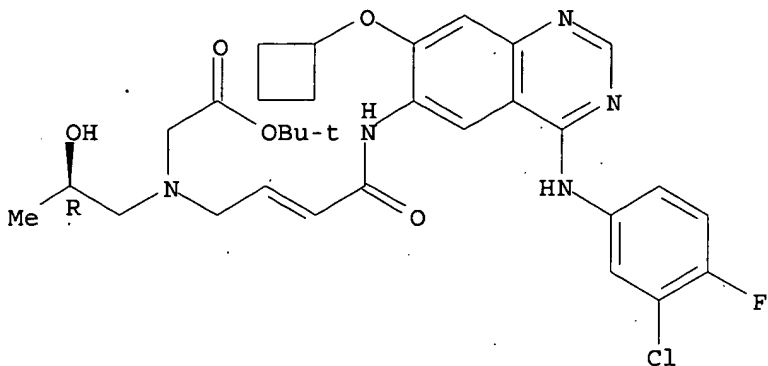
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-21-4 CAPLUS

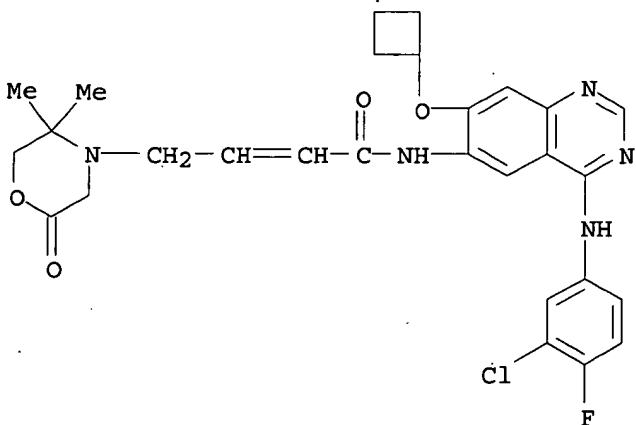
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-22-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

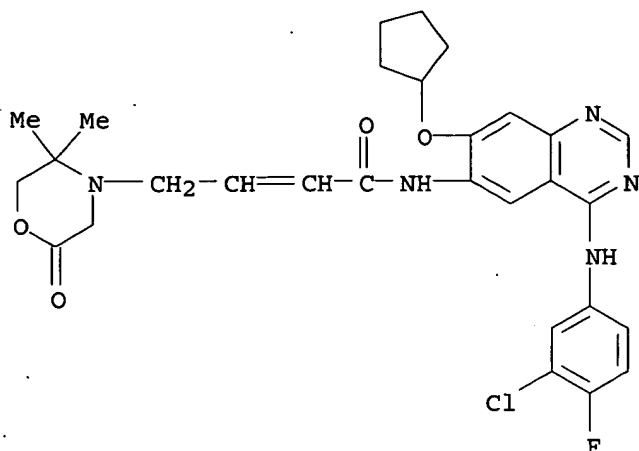


RN 402855-23-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-

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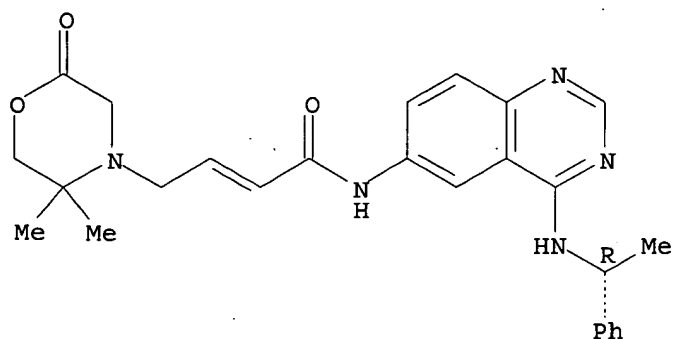
quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 402855-24-7 CAPLUS

CN 2-Butenamide, 4-(5,5-dimethyl-2-oxo-4-morpholinyl)-N-[4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]]- (9CI) (CA INDEX NAME)

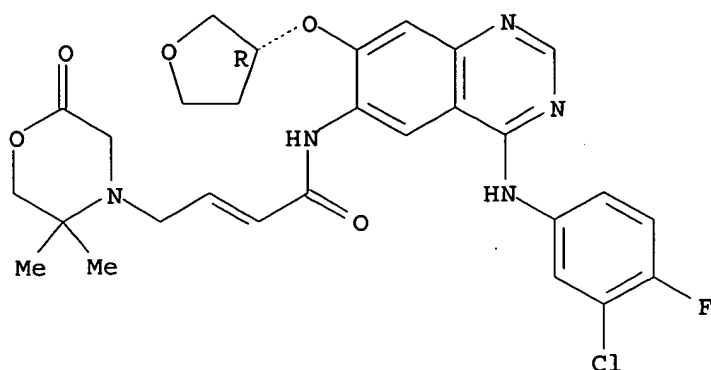
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-25-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)]- (9CI) (CA INDEX NAME)

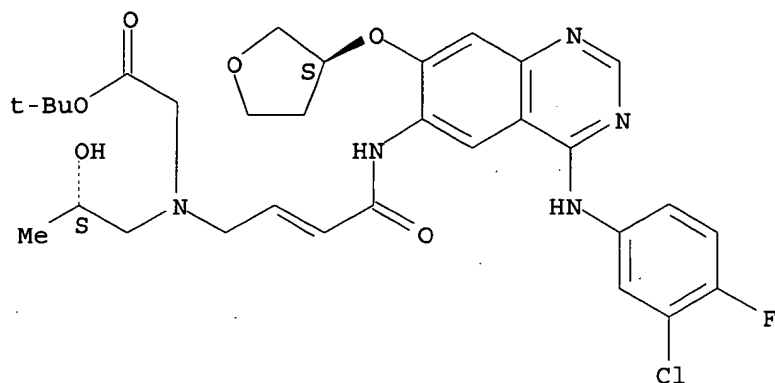
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-26-9 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

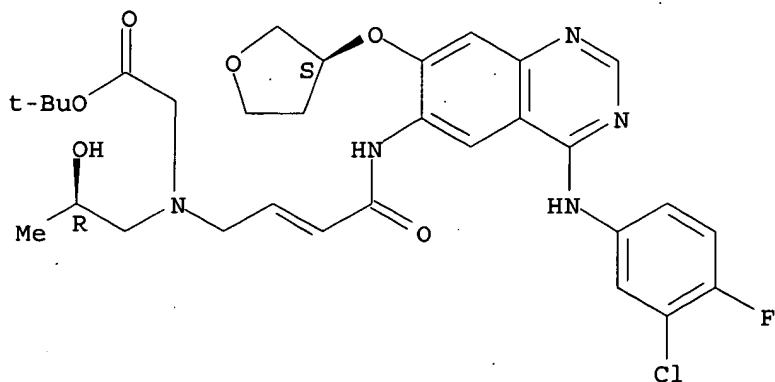
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-27-0 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

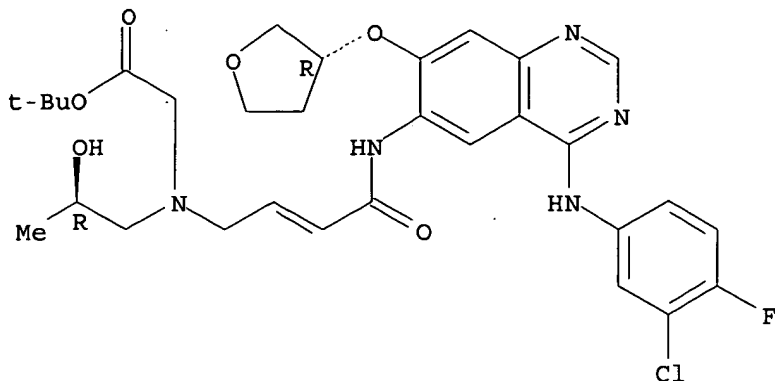


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RN 402855-28-1 CAPLUS

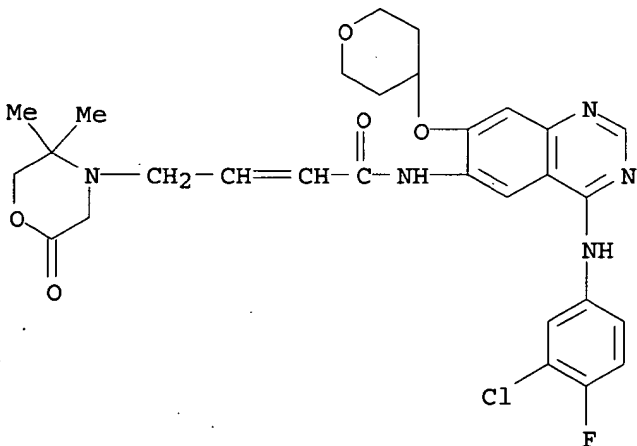
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-29-2 CAPLUS

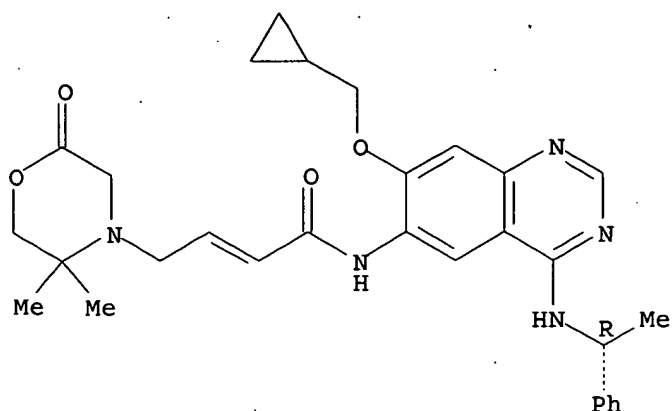
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 402855-30-5 CAPLUS

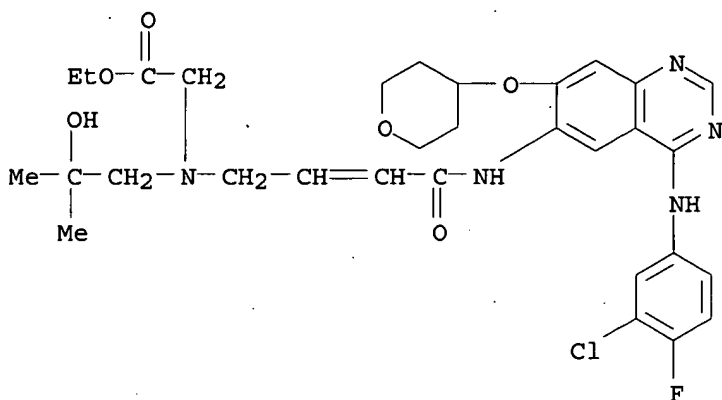
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



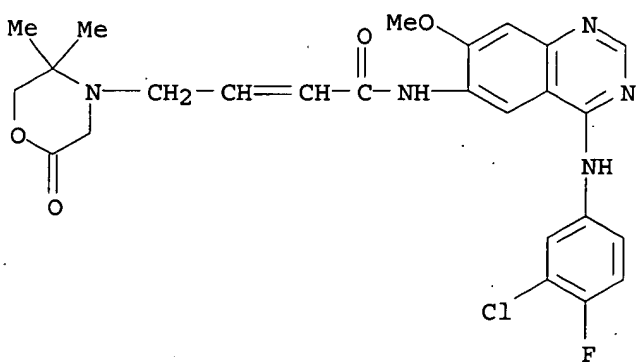
RN 402855-31-6 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 402855-32-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

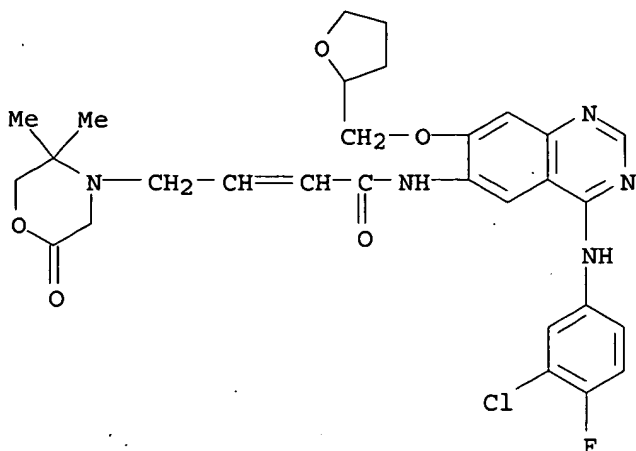


RN 402855-33-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)-

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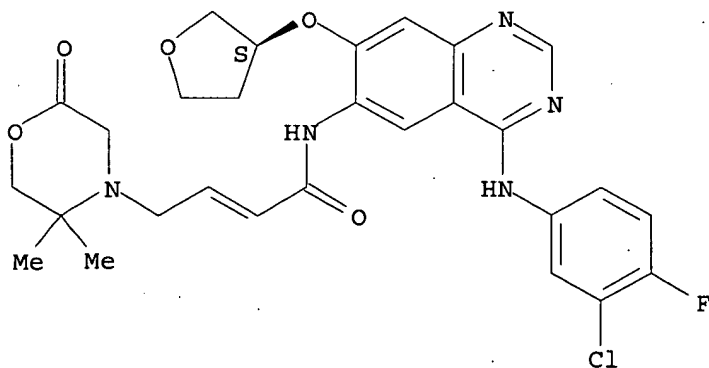
(9CI) (CA INDEX NAME)



RN 402855-34-9 CAPLUS

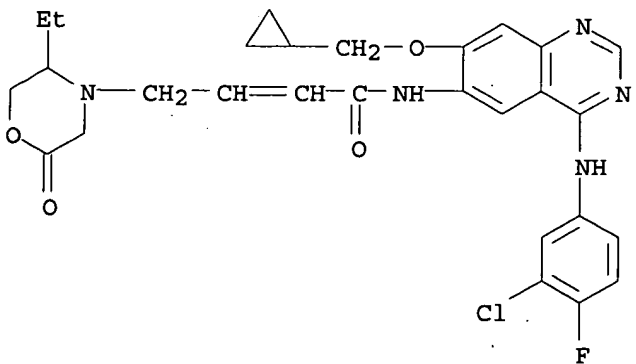
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-35-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5-ethyl-2-oxo-4-morpholinyl)]- (9CI) (CA INDEX NAME)

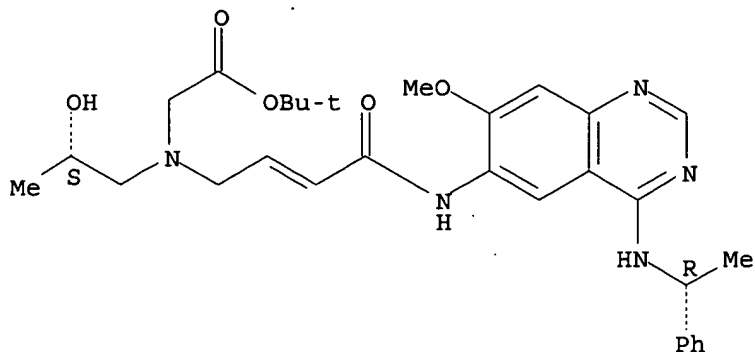


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RN 402855-36-1 CAPLUS

CN Glycine, N-[(2S)-2-hydroxypropyl]-N-[4-[[7-methoxy-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

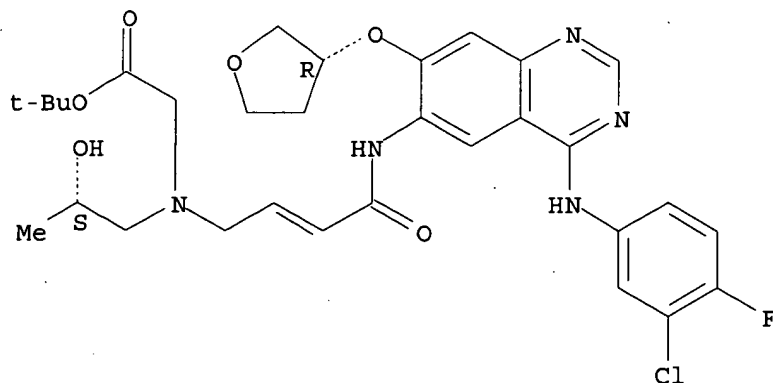
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-37-2 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

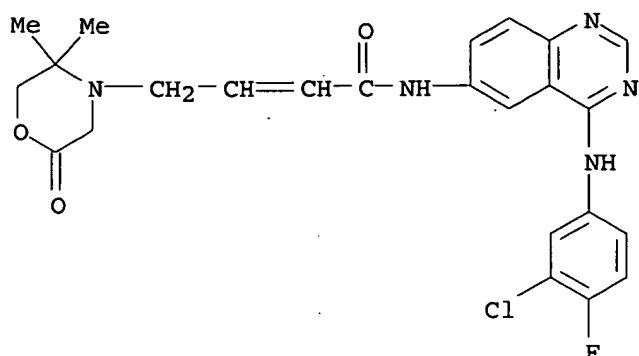
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-38-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

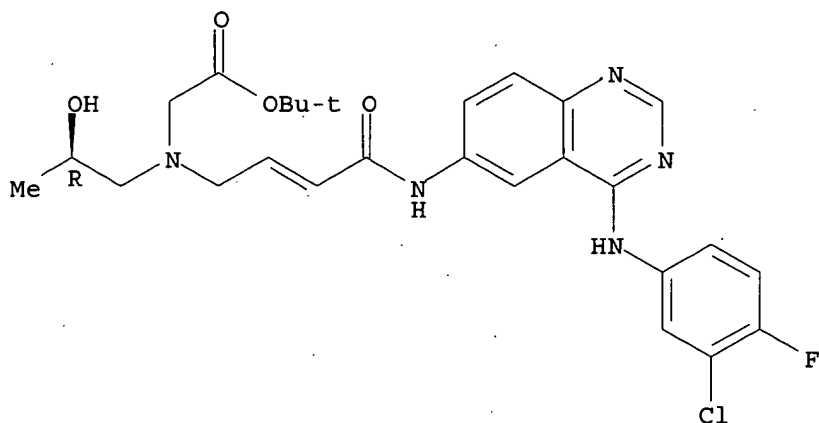
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RN 402855-39-4 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

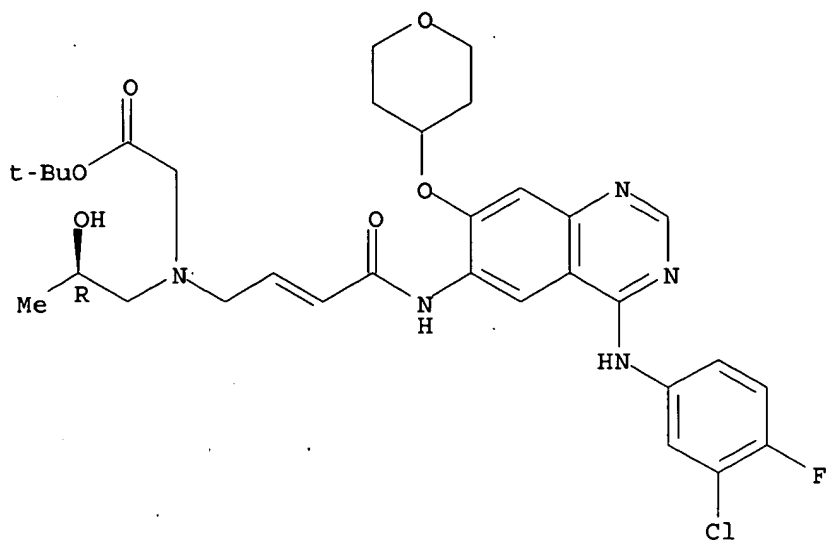


RN 402855-40-7 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

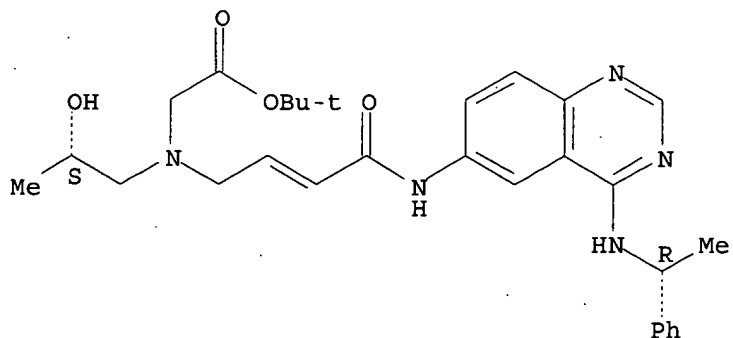
Absolute stereochemistry.
Double bond geometry unknown.

10/ 023,099



RN 402855-41-8 CAPLUS
 CN Glycine, N-[(2S)-2-hydroxypropyl]-N-[4-oxo-4-[[4-[[[(1R)-1-phenylethyl]amino]-2-butenyl]-N-[(2S)-2-hydroxypropyl]-N-(1,1-dimethylethyl)ester (9CI) (CA INDEX NAME)

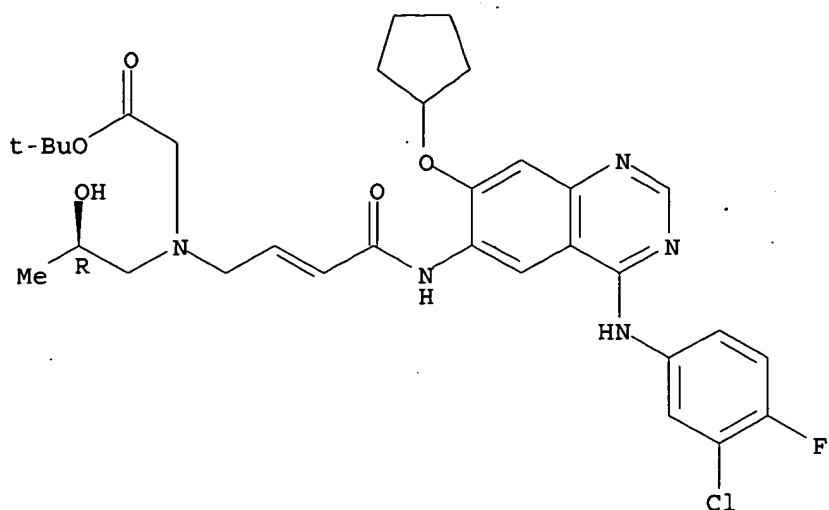
Absolute stereochemistry.
 Double bond geometry unknown.



RN 402855-42-9 CAPLUS
 CN Glycine, N-[4-[[4-[[[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

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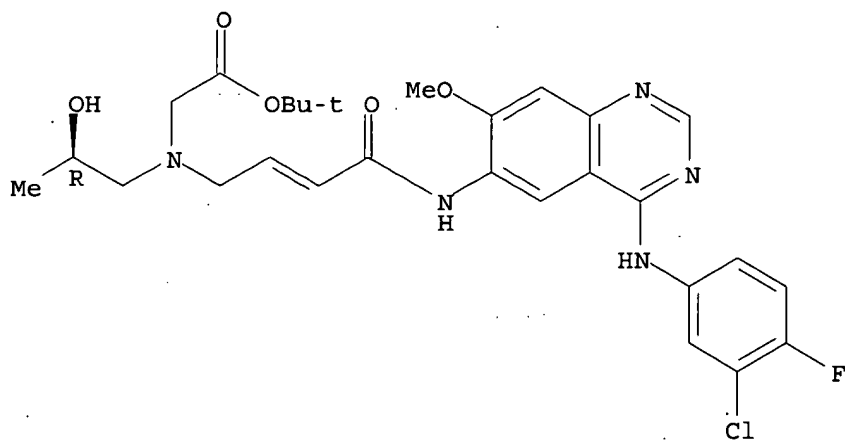


RN 402855-43-0 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

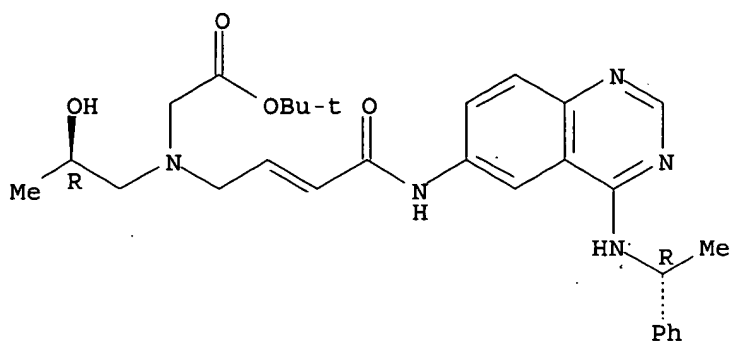


RN 402855-44-1 CAPLUS

CN Glycine, N-[(2R)-2-hydroxypropyl]-N-[4-oxo-4-[[4-[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

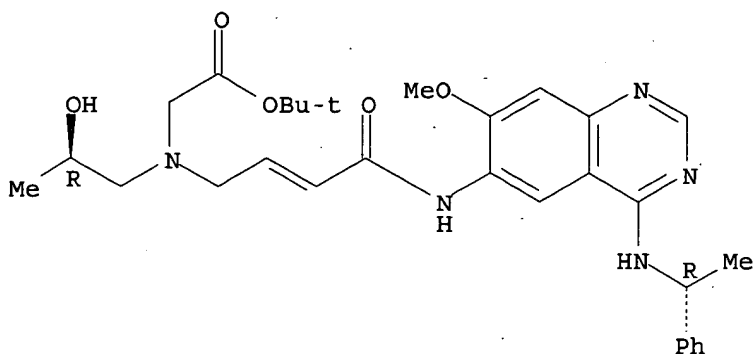
Double bond geometry unknown.



RN 402855-45-2 CAPLUS

CN Glycine, N-[(2R)-2-hydroxypropyl]-N-[4-[[7-methoxy-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

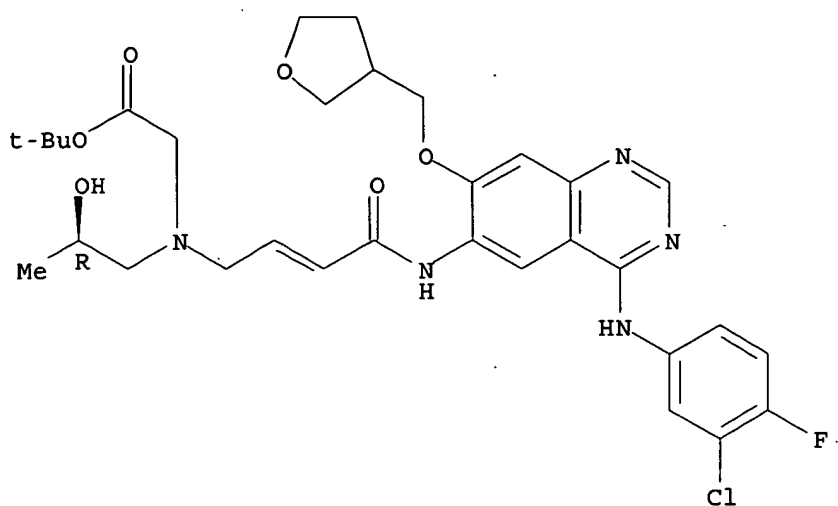
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-46-3 CAPLUS

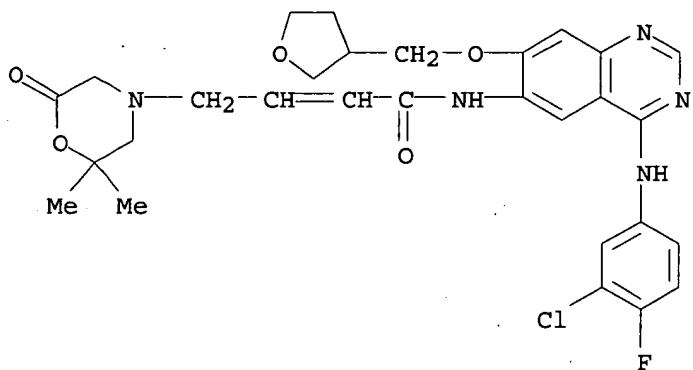
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



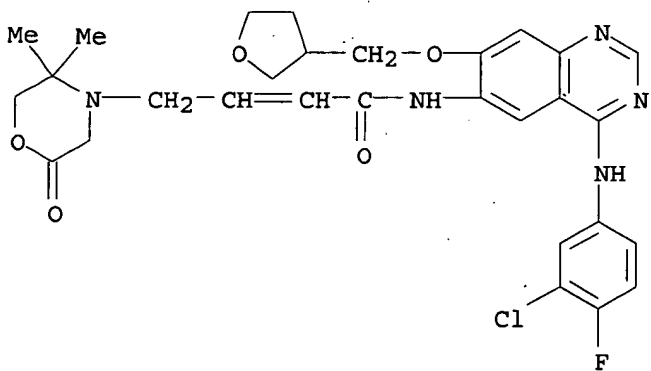
RN 402855-47-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)



RN 402855-48-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)

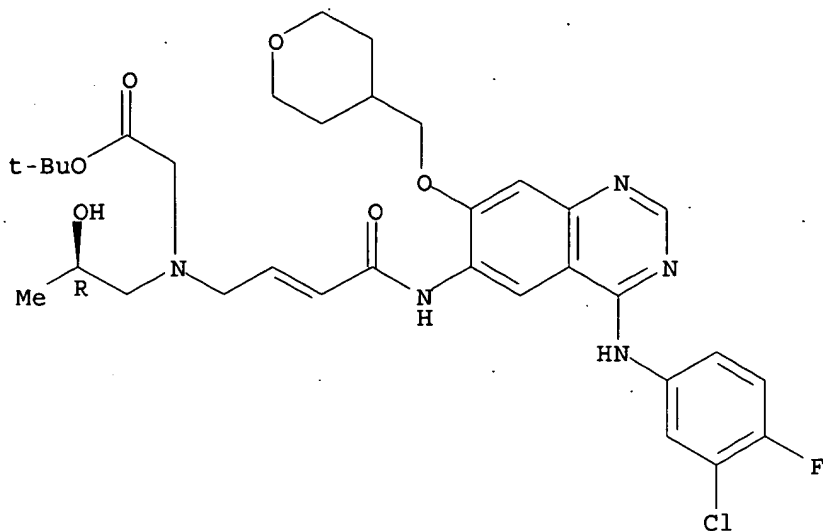


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RN 402855-49-6 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

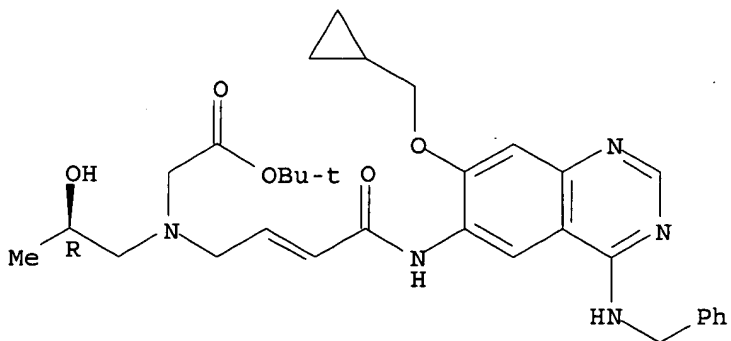
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-50-9 CAPLUS

CN Glycine, N-[4-[[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

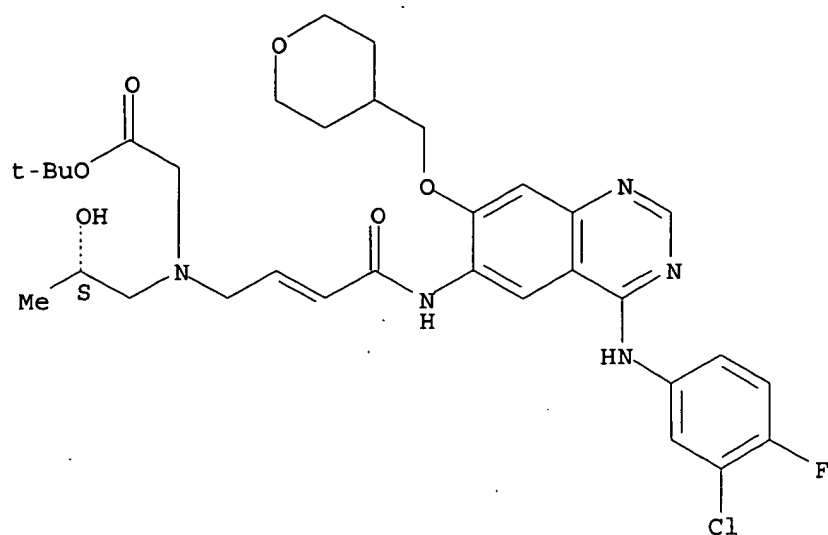


RN 402855-51-0 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

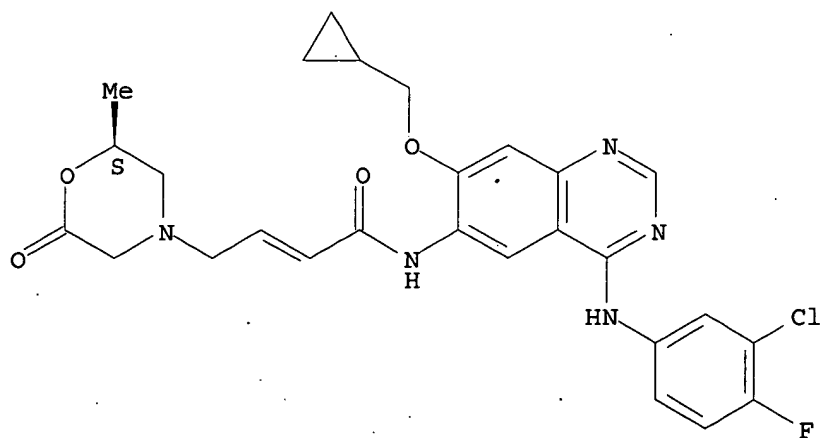
10/ 023,099



RN 402855-52-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

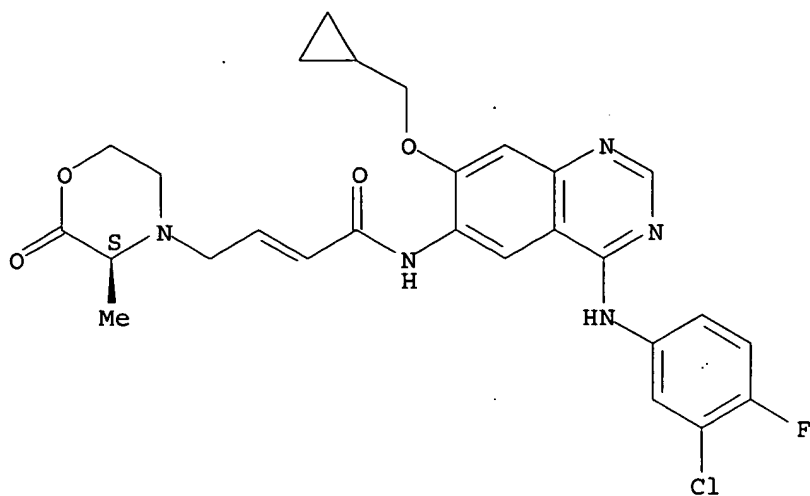
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-54-3 CAPLUS

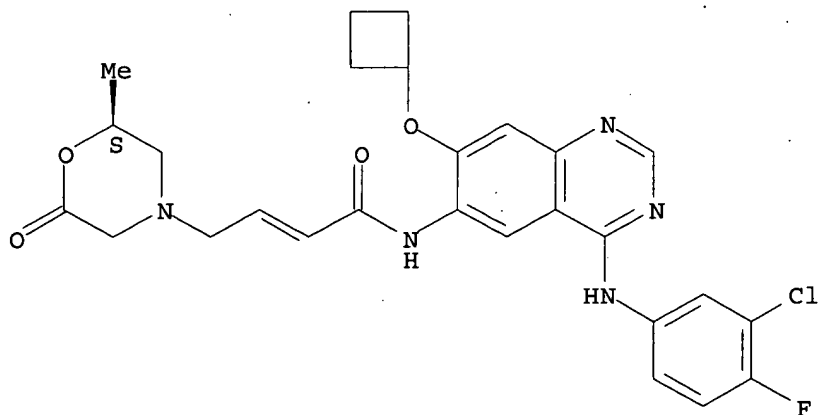
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3S)-3-methyl-2-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



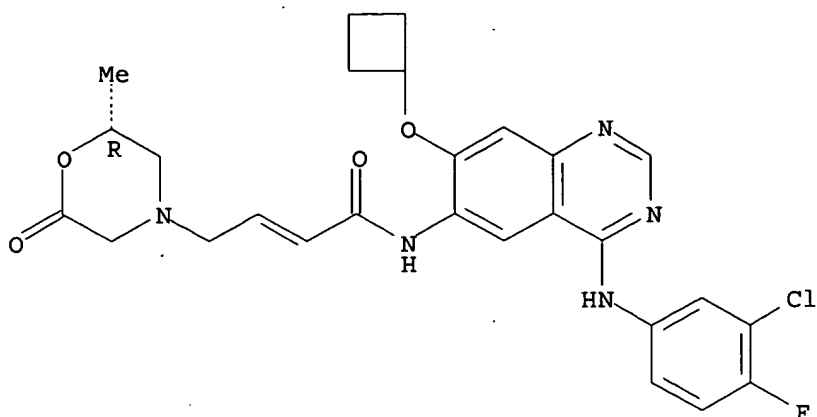
RN 402855-55-4 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.



RN 402855-56-5 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

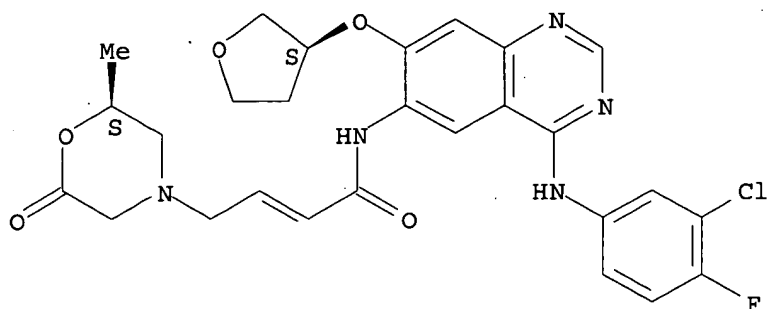
Absolute stereochemistry.
 Double bond geometry unknown.



RN 402855-57-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]]- (9CI)
(CA INDEX NAME)

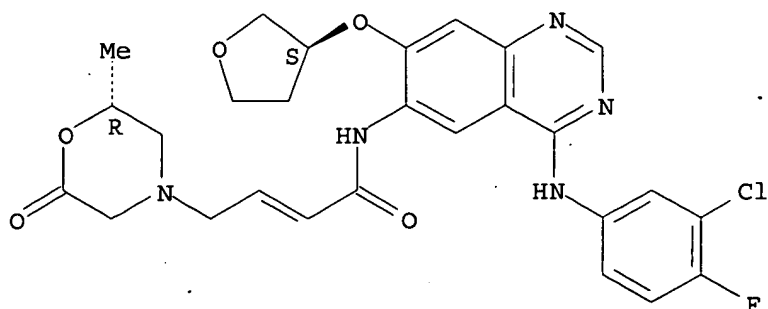
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-58-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



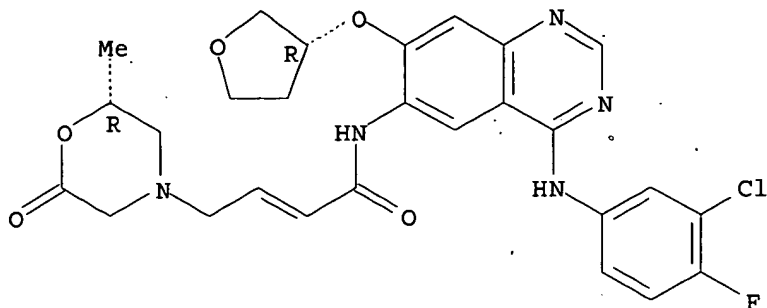
RN 402855-59-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]]- (9CI)

10/ 023,099

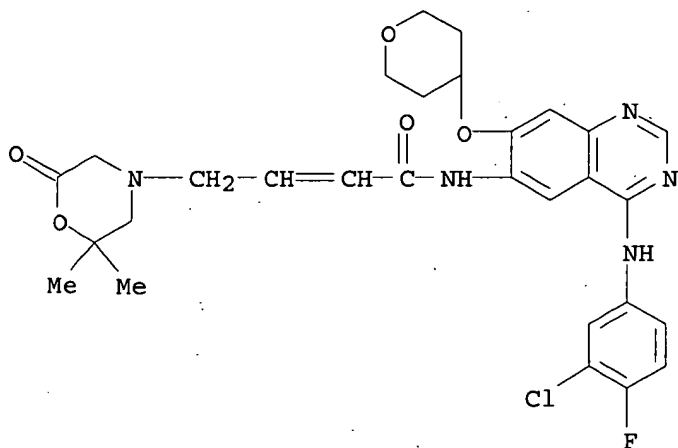
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-60-1 CAPLUS

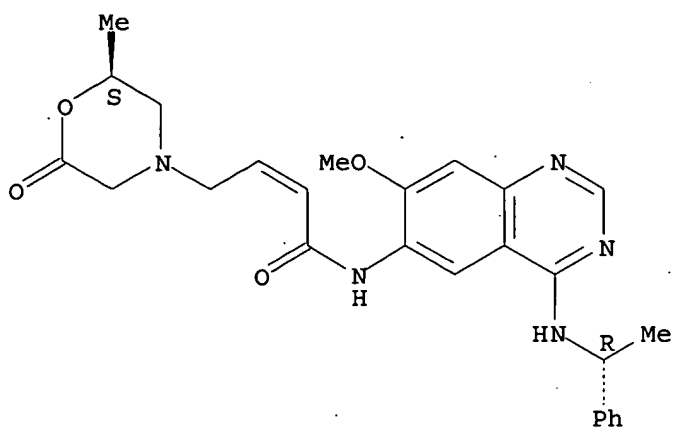
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)



RN 402855-61-2 CAPLUS

CN 2-Butenamide, N-[7-methoxy-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]]-(9CI) (CA INDEX NAME)

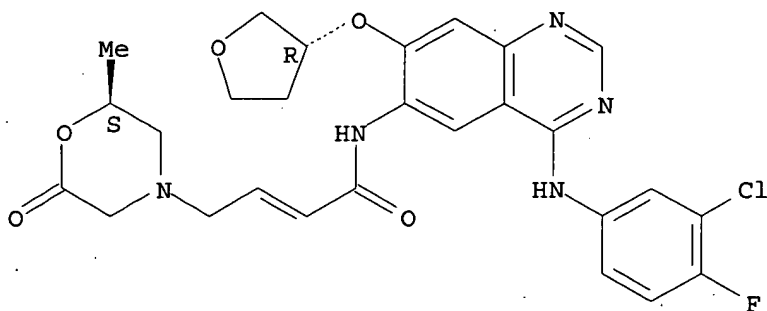
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-62-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]]- (9CI)
(CA INDEX NAME)

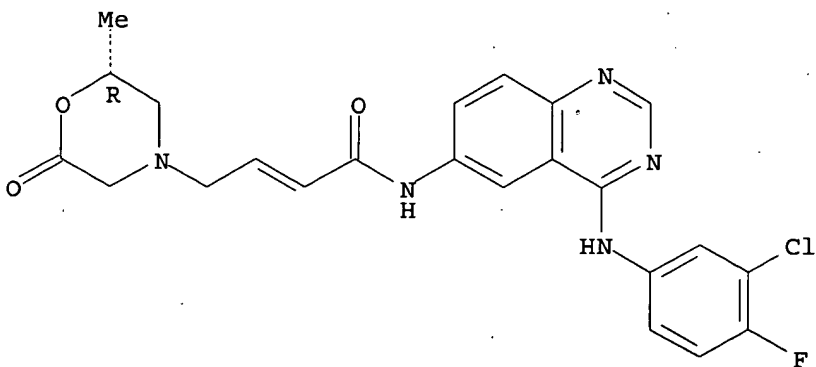
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-63-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



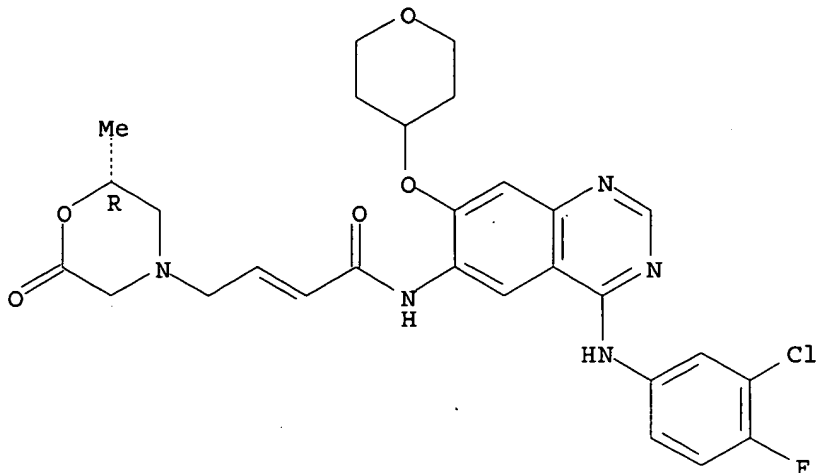
RN 402855-64-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-)]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]]- (9CI)

10/ 023,099

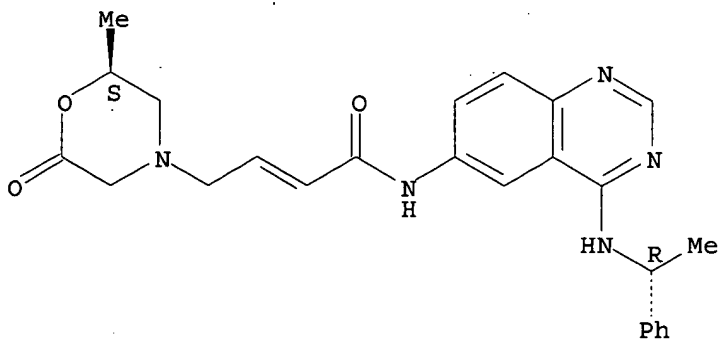
pyran-4-yl)oxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



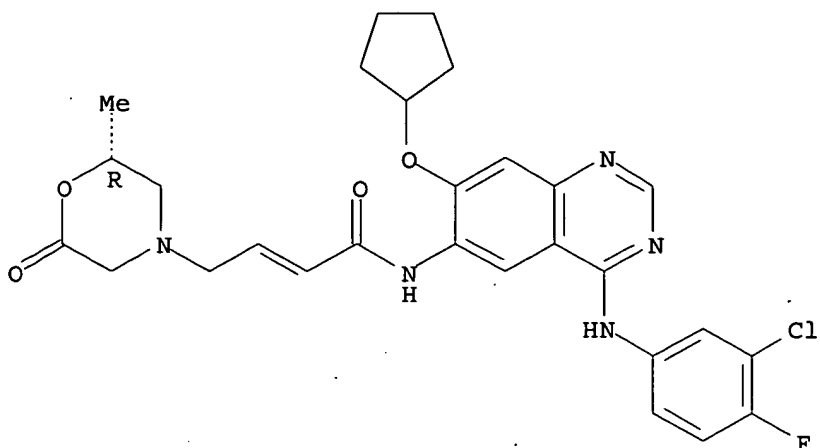
RN 402855-65-6 CAPLUS
CN 2-Butenamide, 4-[(2S)-2-methyl-6-oxo-4-morpholinyl]-N-[4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



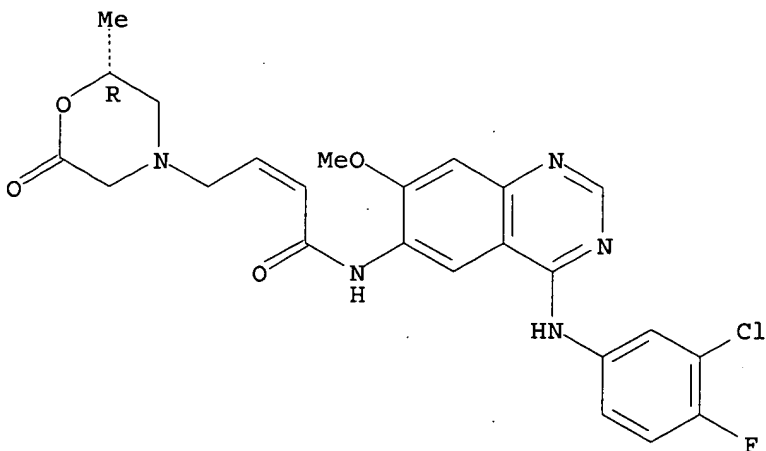
RN 402855-66-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-67-8 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-(9CI) (CA INDEX NAME)

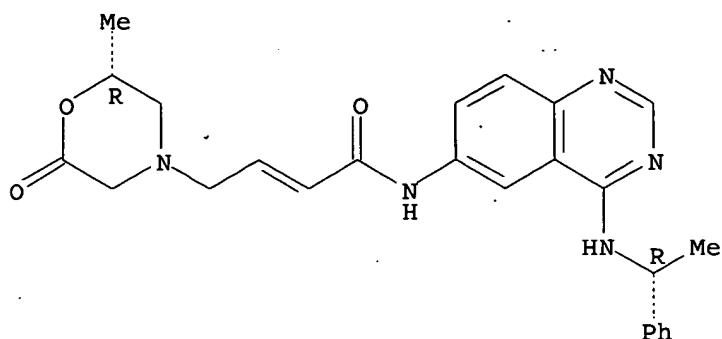
Absolute stereochemistry.
 Double bond geometry unknown.



RN 402855-68-9 CAPLUS
 CN 2-Butenamide, 4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-N-[4-[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

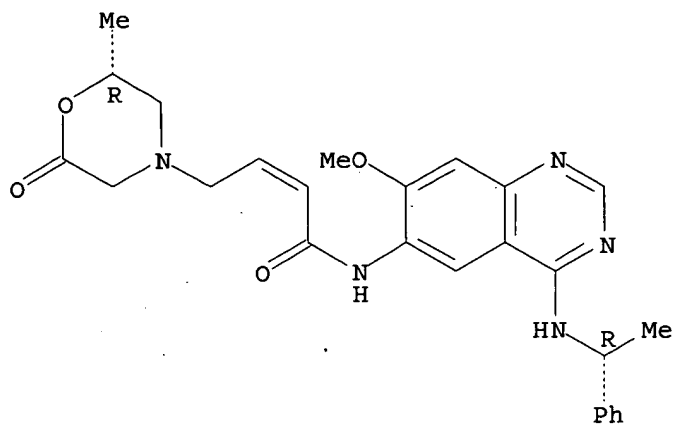
10/ 023,099.



RN 402855-69-0 CAPLUS

CN 2-Butenamide, N-[7-methoxy-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

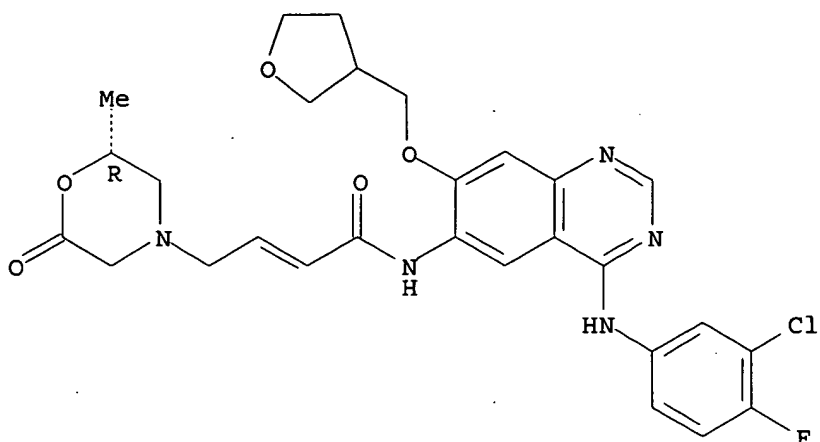
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-70-3 CAPLUS

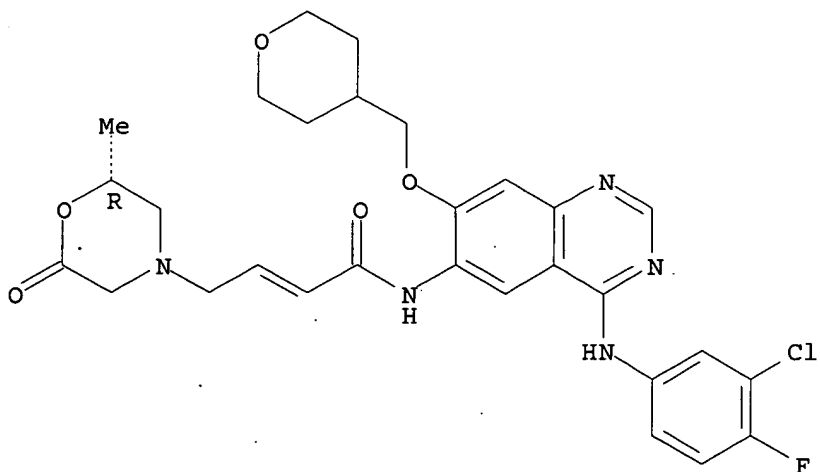
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



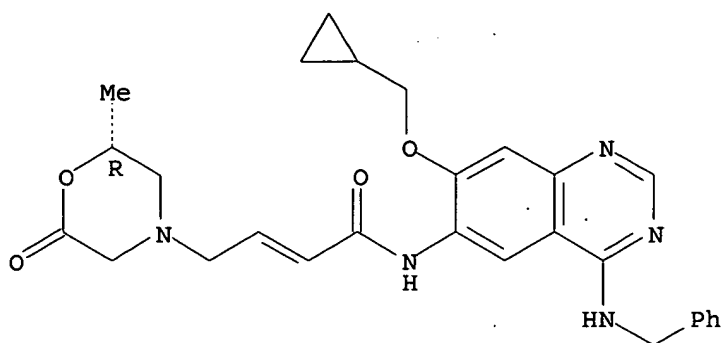
RN 402855-71-4 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.



RN 402855-72-5 CAPLUS
 CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

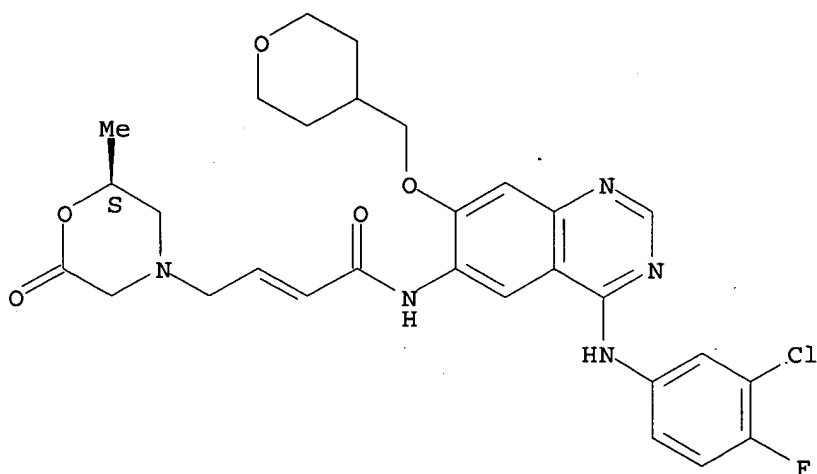
Absolute stereochemistry.
 Double bond geometry unknown.



RN 402855-73-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

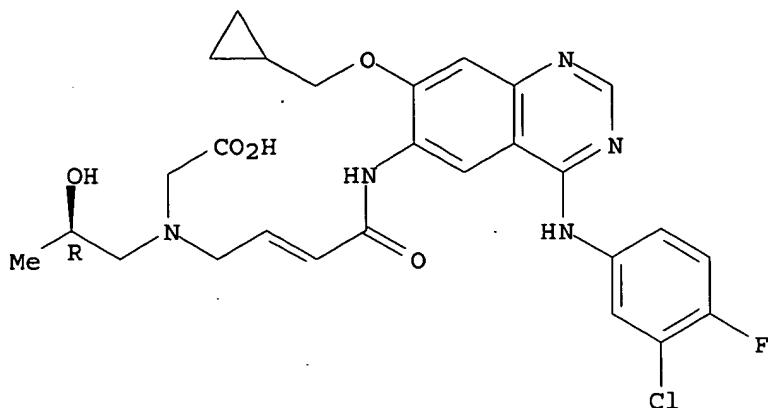
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-74-7 CAPLUS

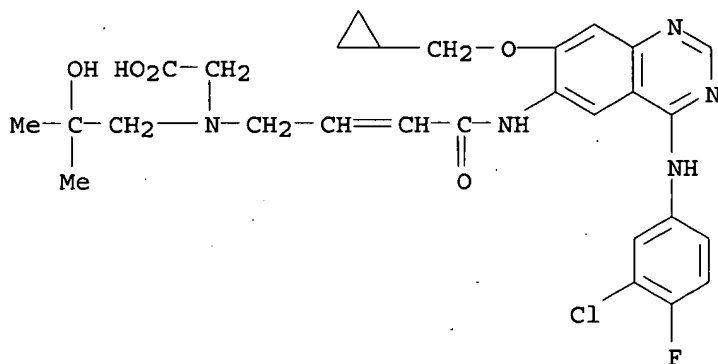
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



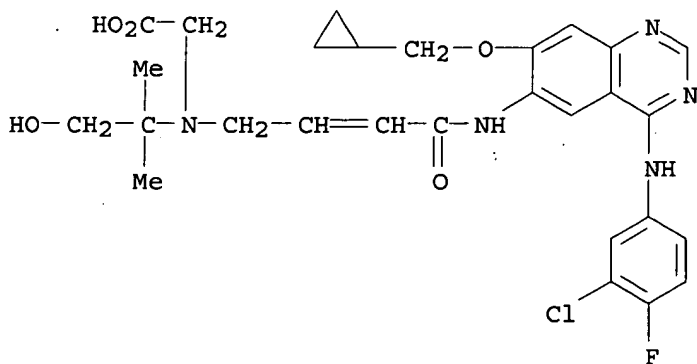
RN 402855-75-8 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)- (9CI)
(CA INDEX NAME)



RN 402855-76-9 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



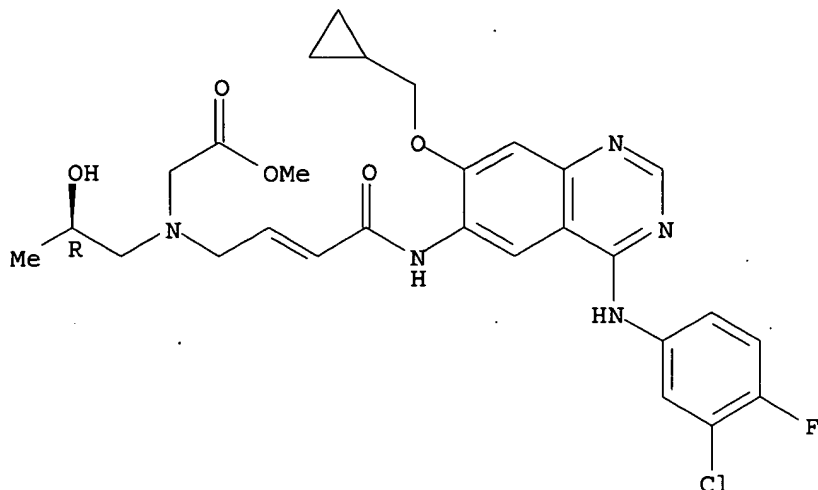
RN 402855-77-0 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, methyl

10/ 023,099

ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



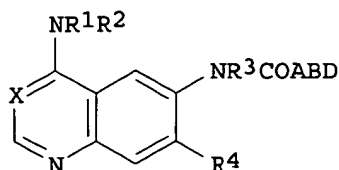
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:762992 CAPLUS
DOCUMENT NUMBER: 135:303907
TITLE: Preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction.
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
DE 10017539	A1	20011011	DE 2000-10017539	20000408
DE 10040525	A1	20020228	DE 2000-10040525	20000818
EP 1280798	A1	20030205	EP 2001-938076	20010331
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRIORITY APPLN. INFO.:			DE 2000-10017539 A	20000408
			DE 2000-10040525 A	20000818
			WO 2001-EP3694 W	20010331

OTHER SOURCE(S):
GI

MARPAT 135:303907



I

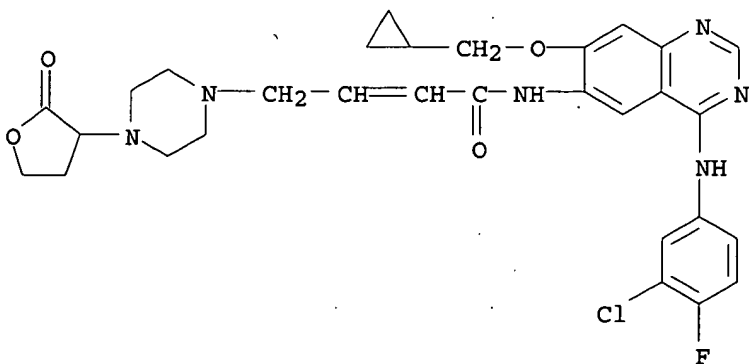
AB Title compds. [I; X = NCN, N; R1 = H, alkyl; R2 = (substituted) Ph, PhCH2, PhCH2CH2; R3 = H, alkyl; R4 = H, alkoxy, cycloalkoxy, cycloalkylalkoxy; A = (substituted) vinylene; B = bond, (fluoro)alkylene; D = substituted pyrrolidinyl, piperidinyl, piperazinyl, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-(piperazin-1-yl)-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline (prepn. given) in THF was treated with Et3N and then with 3-bromodihydrofuran-2-one in THF under ice cooling followed by stirring for 48 h at room temp. to give 56% 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-[4-(2-oxotetrahydrofuran-3-yl)piperazin-1-yl]-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERC cells with IC50 = 0.05 nM.

IT 365532-35-0P 365532-36-1P 365532-37-2P
365532-39-4P 365532-41-8P 365532-42-9P
365532-44-1P 365532-45-2P 365532-46-3P
365532-47-4P 365532-48-5P 365532-49-6P
367282-07-3P 367282-12-0P 367282-15-3P
367282-23-3P 367282-25-5P 367282-27-7P
367282-29-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN. (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

RN 365532-35-0 CAPLUS

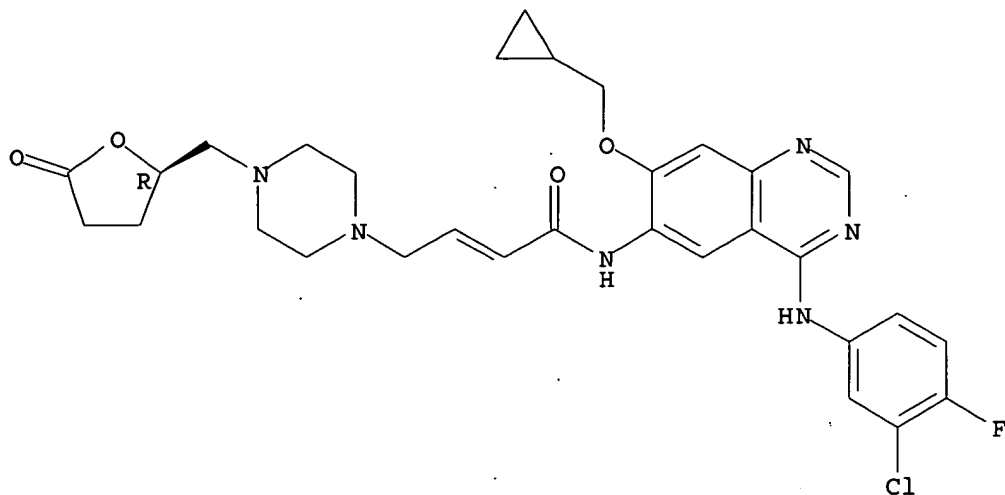
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperazinyl]- (9CI)
(CA INDEX NAME)



RN 365532-36-1 CAPLUS

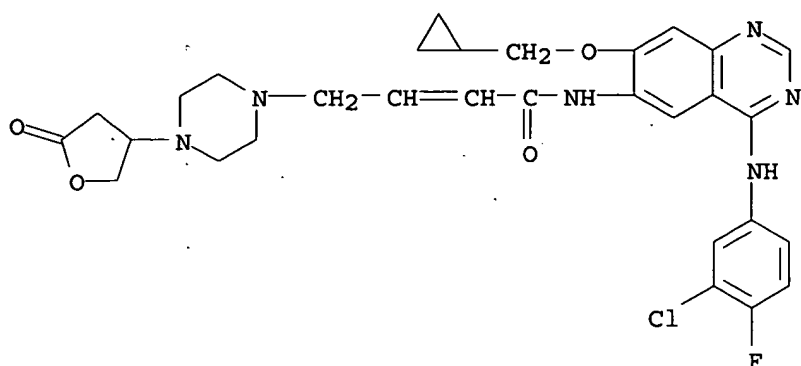
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[[2R]-tetrahydro-5-oxo-2-furanyl]methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

CN1CCCCC1N(C)C2=CC(=O)OC2CC3=CC=C(C=C3NC4=CC=C(C=C4)N5C=NC6=CC=CC=C65)C(=O)C=CCN7C8=CC=CC=C8C(F)=CC(Cl)=C8C9=CC=CC=C9OC91C=CC=CC1

RN	365532-39-4	CAPLUS
CN	2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-5-oxo-3-furanyl)-1-piperazinyl]- (9CI)	
	(CA INDEX NAME)	

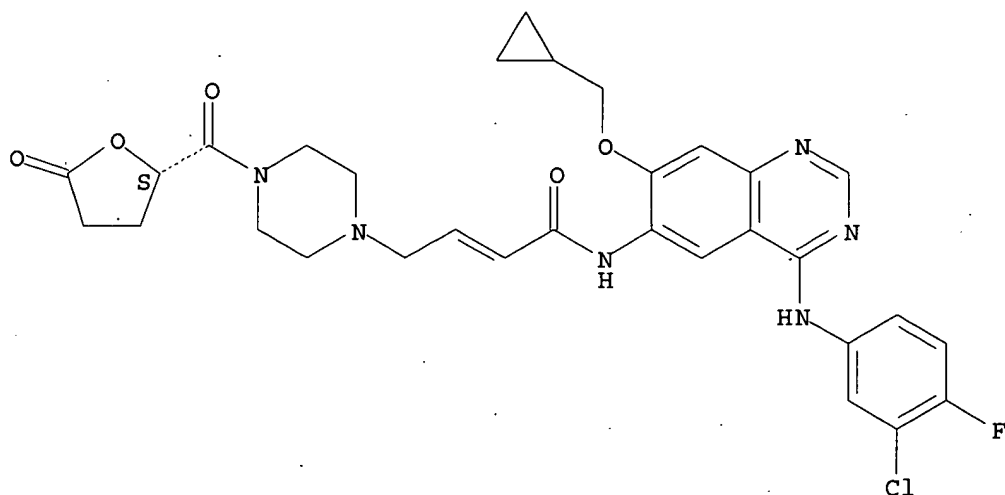
10/ 023,099



RN 365532-41-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-1-piperazinyl]- (9CI). (CA INDEX NAME)

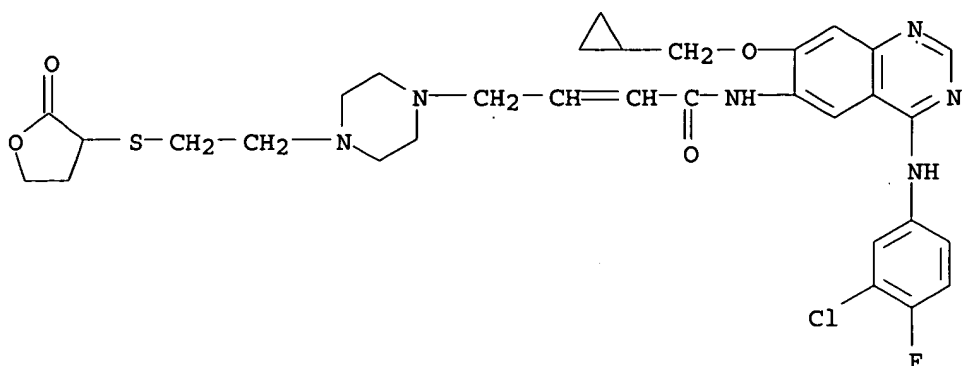
Absolute stereochemistry.
Double bond geometry unknown.



RN 365532-42-9 CAPLUS

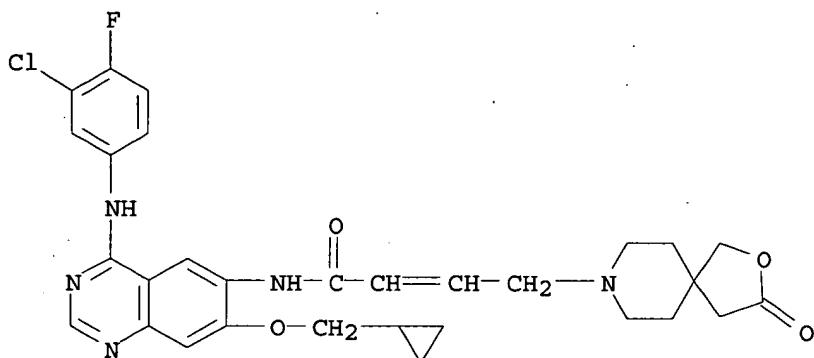
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[2-[(tetrahydro-2-oxo-3-furanyl)thio]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

10/ 023,099



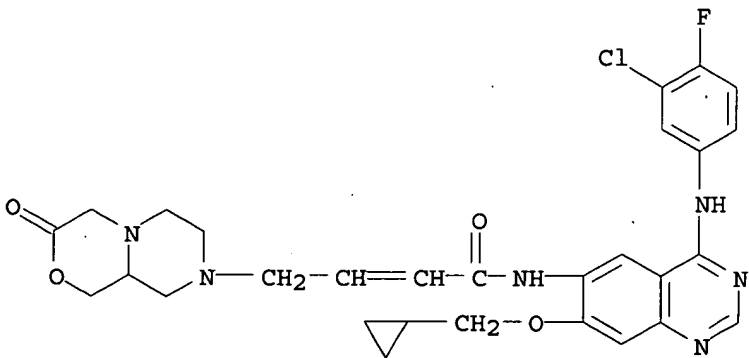
RN 365532-44-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(3-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)



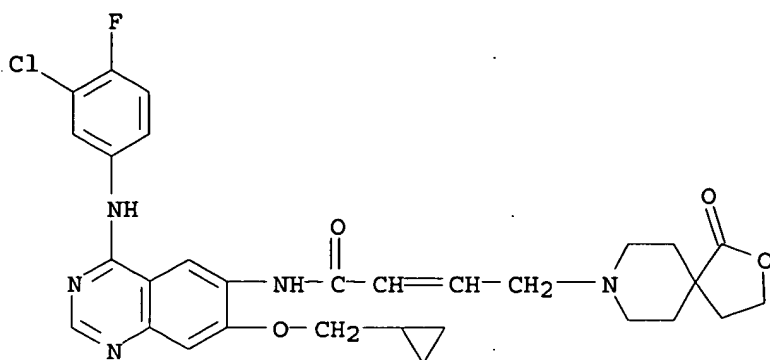
RN 365532-45-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-3-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)- (9CI) (CA INDEX NAME)



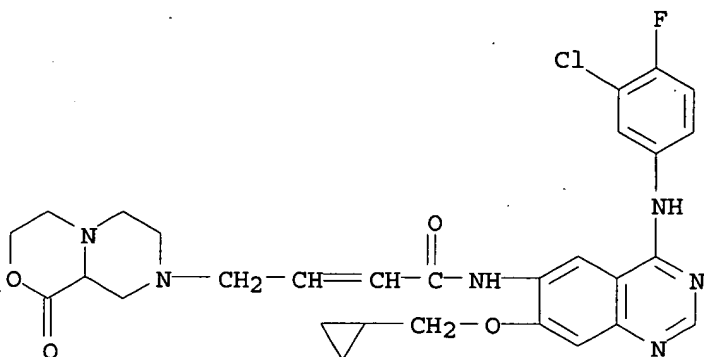
RN 365532-46-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)



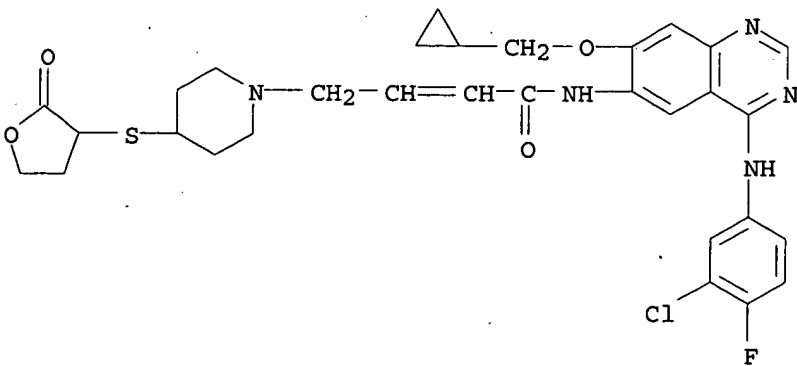
RN 365532-47-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(hexahydro-1-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)



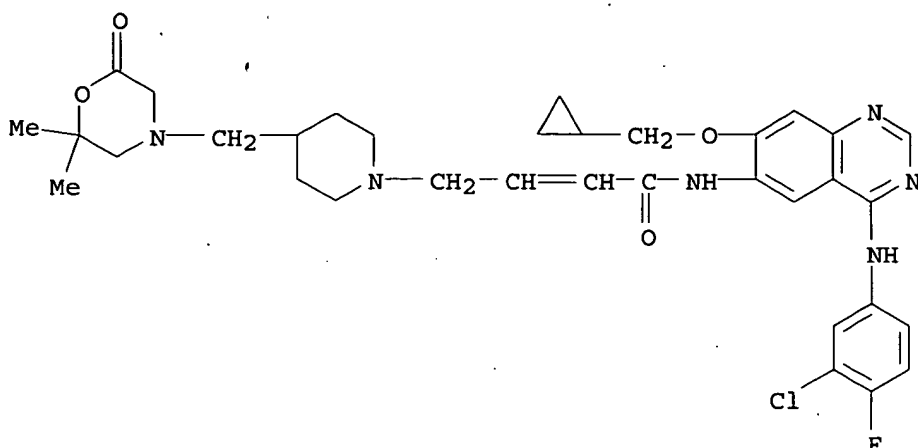
RN 365532-48-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(tetrahydro-2-oxo-3-furanylthio)-1-piperidinyl]-(9CI) (CA INDEX NAME)



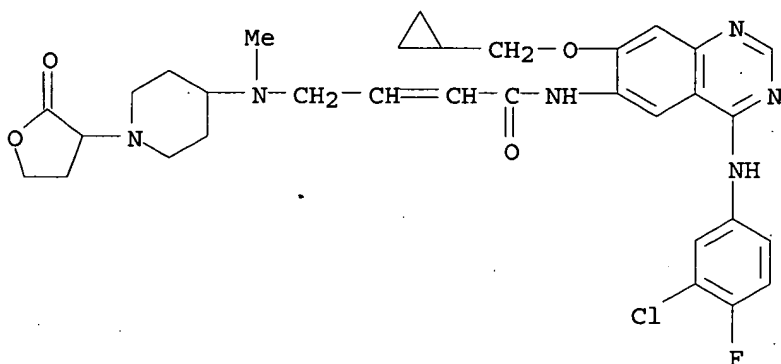
RN 365532-49-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]-(9CI) (CA INDEX NAME)



RN 367282-07-3 CAPLUS

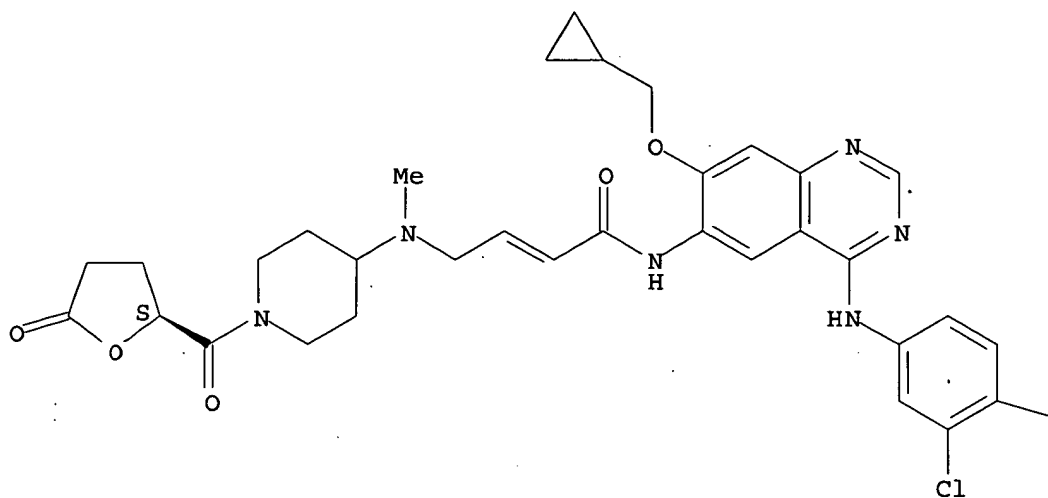
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[1-(tetrahydro-2-oxo-3-furanyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)



RN 367282-12-0 CAPLUS

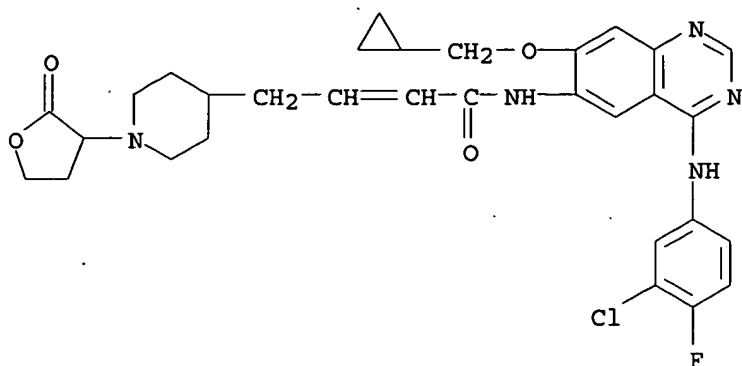
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[1-[[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



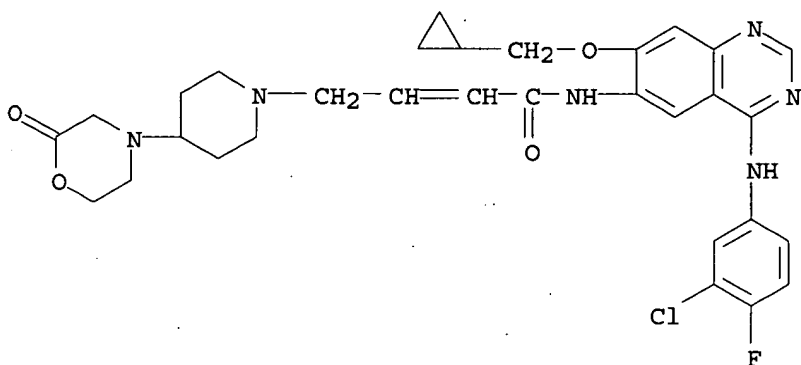
F

RN 367282-15-3 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[1-(tetrahydro-2-oxo-3-furanyl)-4-piperidinyl]- (9CI)
 (CA INDEX NAME)



RN 367282-23-3 CAPLUS

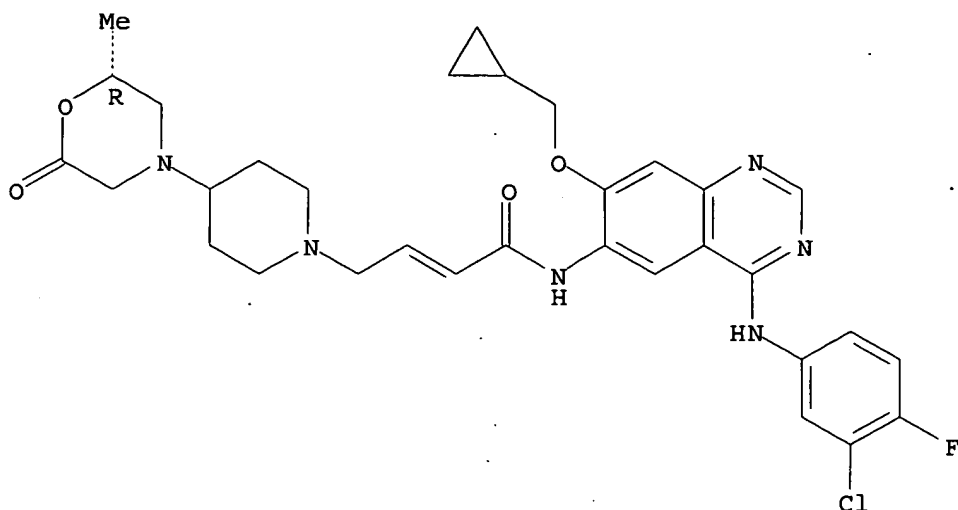
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(2-oxo-4-morpholinyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)



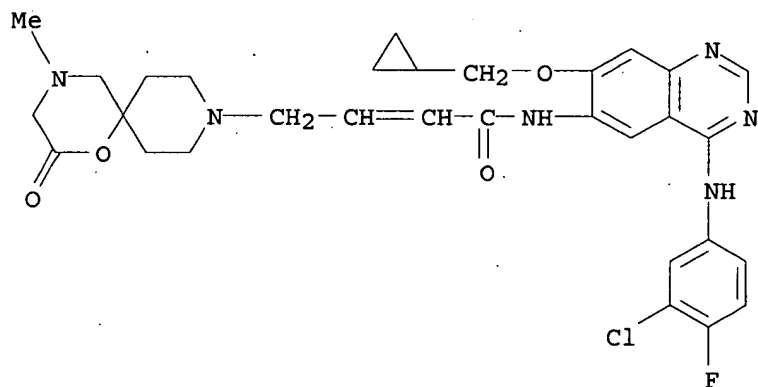
RN 367282-25-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)

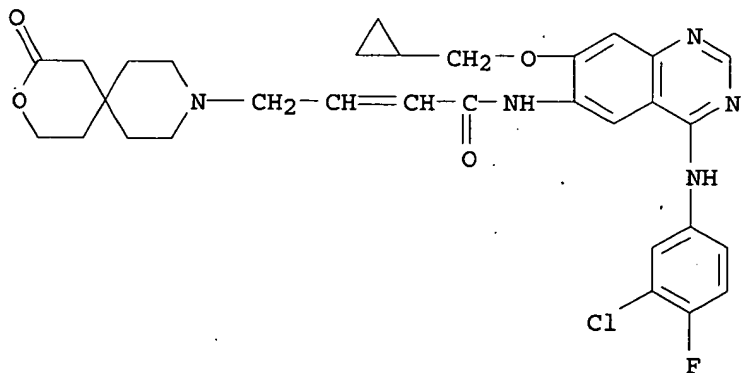
Absolute stereochemistry.
Double bond geometry unknown.



RN 367282-27-7 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-methyl-2-oxo-1-oxa-4,9-diazaspiro[5.5]undec-9-yl)- (9CI) (CA INDEX NAME)



RN 367282-29-9 CAPLUS
 CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-3-oxa-9-azaspiro[5.5]undec-9-yl)- (9CI) (CA INDEX NAME)



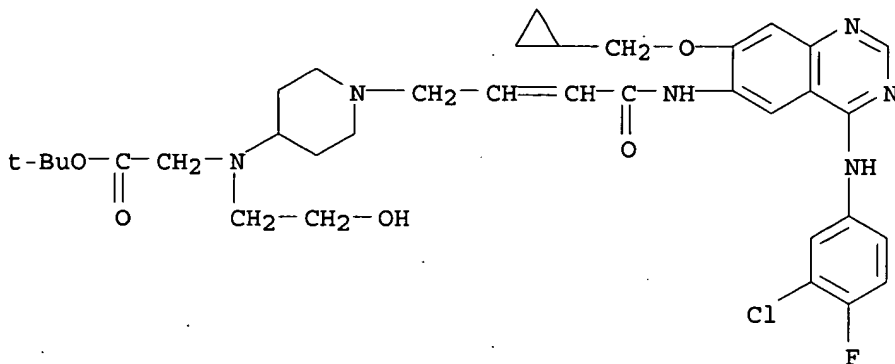
IT 367283-05-4 367283-07-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

RN 367283-05-4 CAPLUS

CN Glycine, N-[1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]-N-(2-hydroxyethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

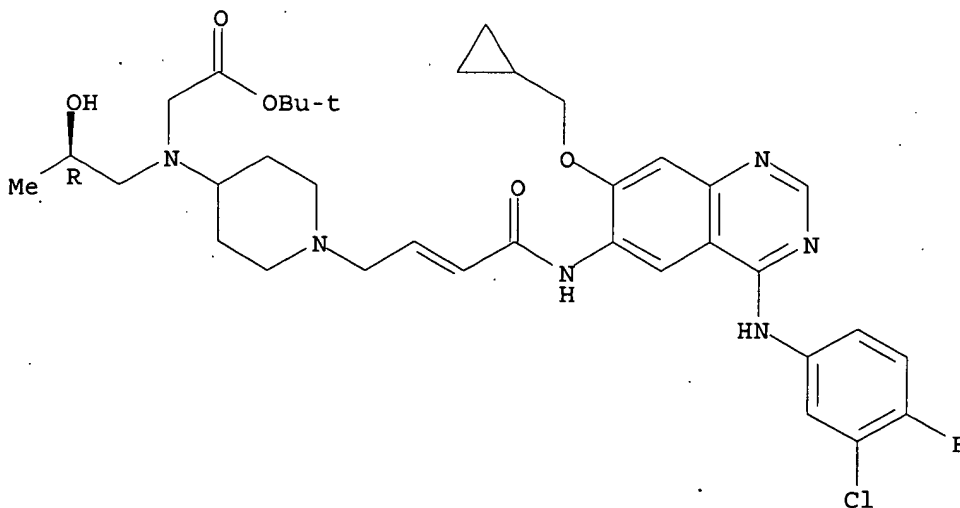


RN 367283-07-6 CAPLUS

CN Glycine, N-[1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



IT 290303-47-8P 290304-01-7P 365532-06-5P

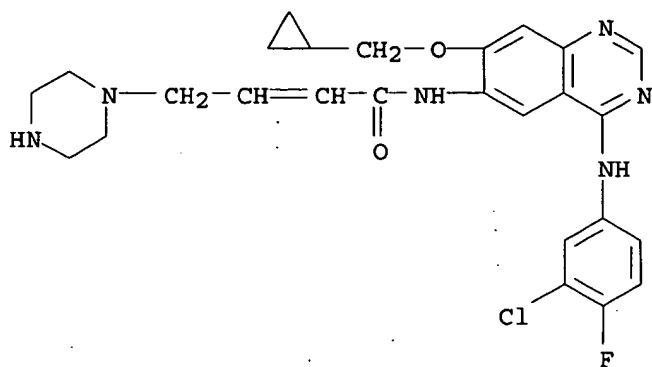
365532-18-9P 367282-36-8P 367282-44-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

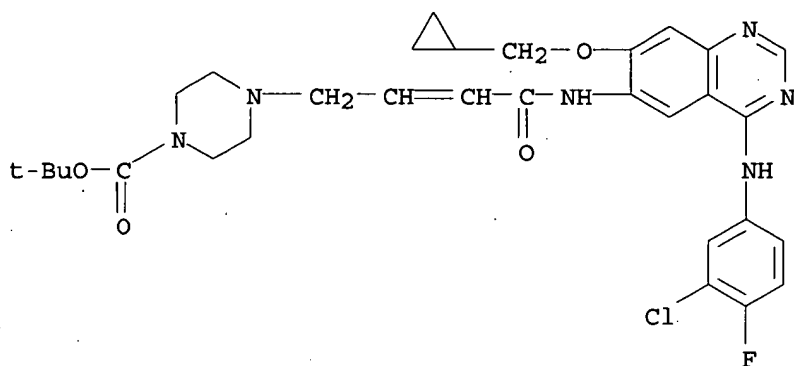
RN 290303-47-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)



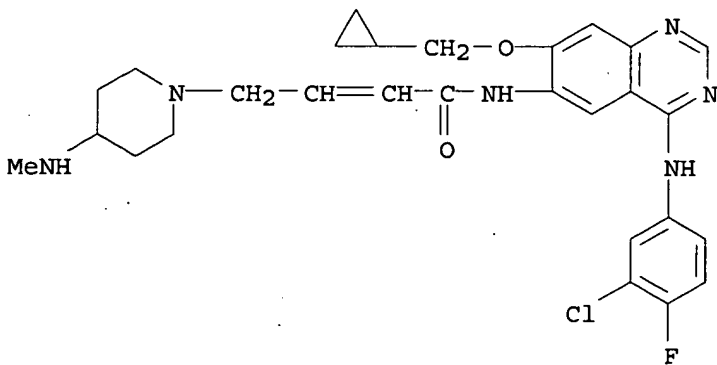
RN 290304-01-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



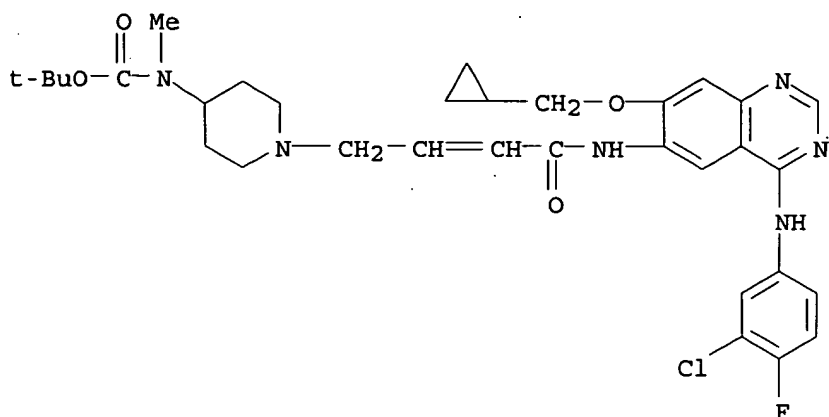
RN 365532-06-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(methylamino)-1-piperidiny]- (9CI) (CA INDEX NAME)



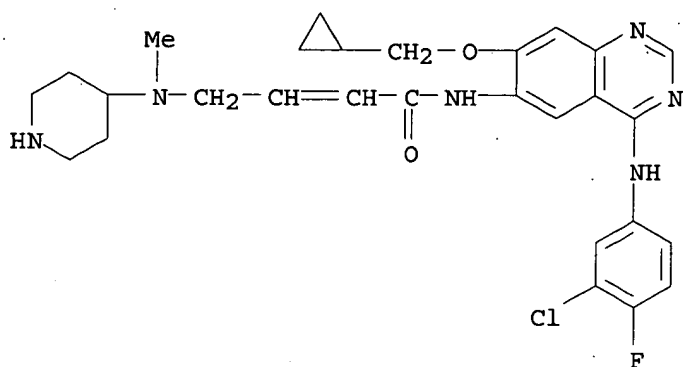
RN 365532-18-9 CAPLUS

CN Carbamic acid, [1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidiny]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



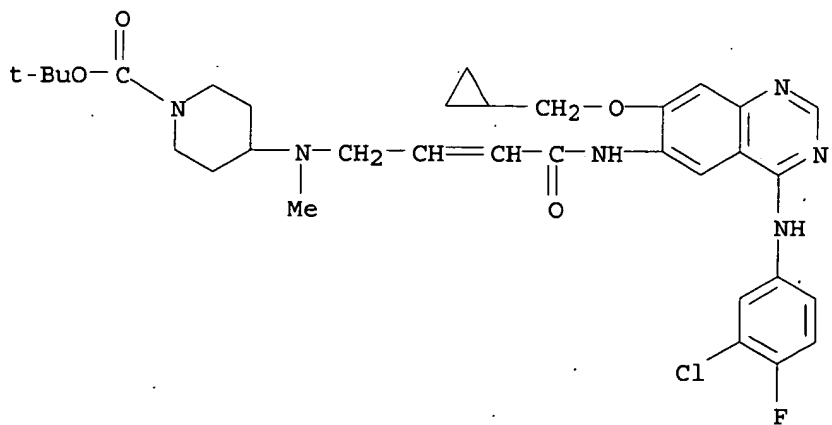
RN 367282-36-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(methyl-4-piperidinylamino)- (9CI) (CA INDEX NAME)



RN 367282-44-8 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:747043 CAPLUS

DOCUMENT NUMBER: 135:303901

TITLE: Bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany

SOURCE: Ger. Offen., 28 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10017539	A1	20011011	DE 2000-10017539	20000408
US 2001044435	A1	20011122	US 2001-816003	20010323
WO 2001077104	A1	20011018	WO 2001-EP3694	20010331

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

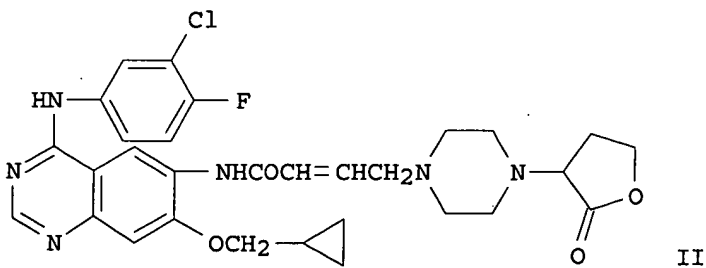
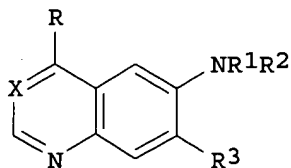
EP 1280798 A1 20030205 EP 2001-938076 20010331

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: DE 2000-10017539 A 20000408
DE 2000-10040525 A 20000818
WO 2001-EP3694 W 20010331

OTHER SOURCE(S): MARPAT 135:303901

GI



AB Bicyclic heterocycles I [X = N, CCN; R = substituted NH2; R1 = H, alkyl; R2 = acyl; R3 = H, (un)substituted alkoxy, cycloalkoxy,

tetrahydrofuranyloxy, tetrahydropyranyloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy] were prepd. for use as inhibitors of tyrosine kinase-mediated signal transduction for treatment of tumors and diseases of the lung and airway. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-7-fluoro-6-nitroquinazoline was treated with cyclopropylmethanol, followed by redn. to the amine, reaction with 4-bromocrotonic acid and N-tert.-butoxycarbonylpiperazine, and deblocking to give the quinazoline II. II had an IC50 for inhibition of epidermal growth factor dependent proliferation of 0.05 nM.

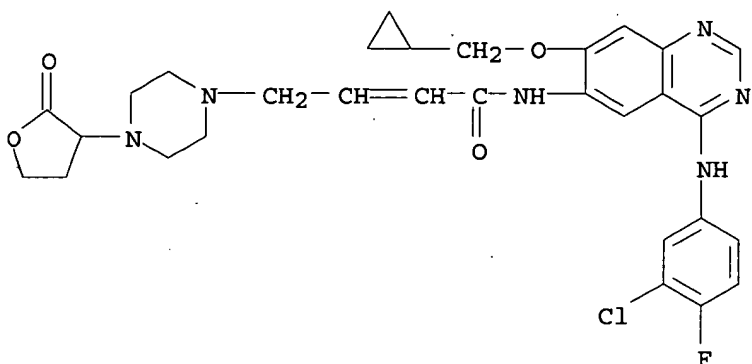
IT 365532-35-0P 365532-39-4P 365532-42-9P
365532-45-2P 365532-47-4P 365532-48-5P
365532-49-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

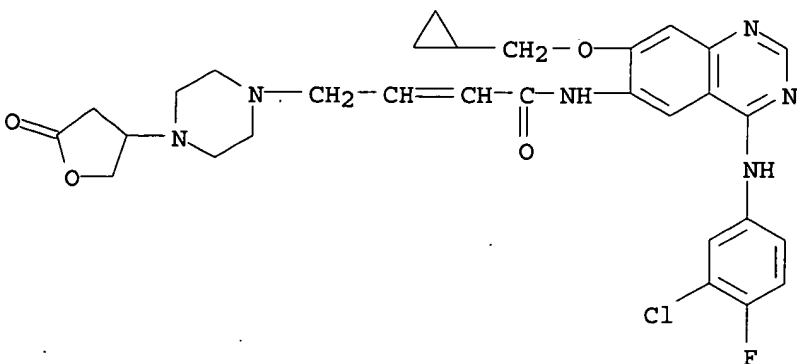
RN 365532-35-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperazinyl]- (9CI)
(CA INDEX NAME)



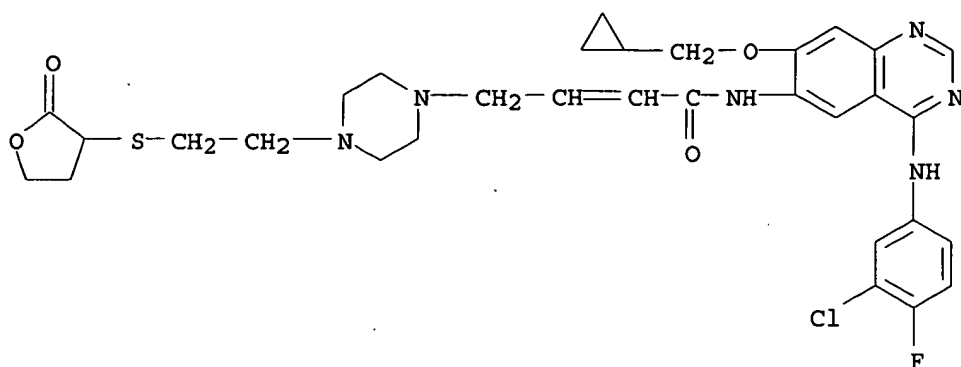
RN 365532-39-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-5-oxo-3-furanyl)-1-piperazinyl]- (9CI)
(CA INDEX NAME)



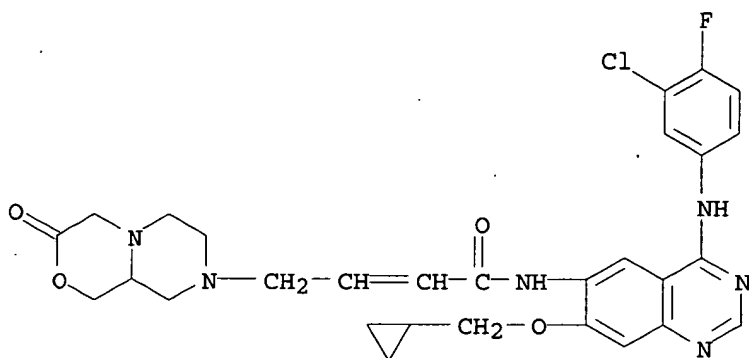
RN 365532-42-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[2-[(tetrahydro-2-oxo-3-furanyl)thio]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



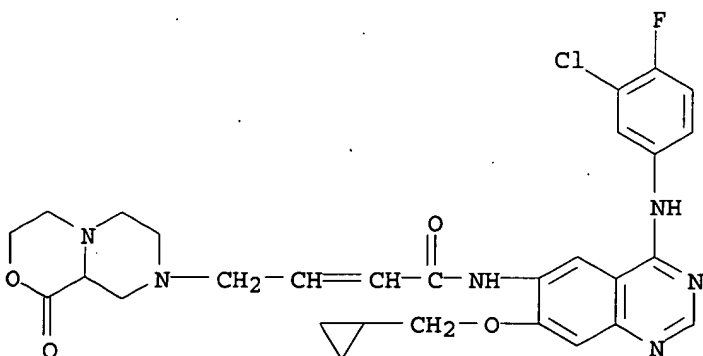
RN 365532-45-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-3-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)



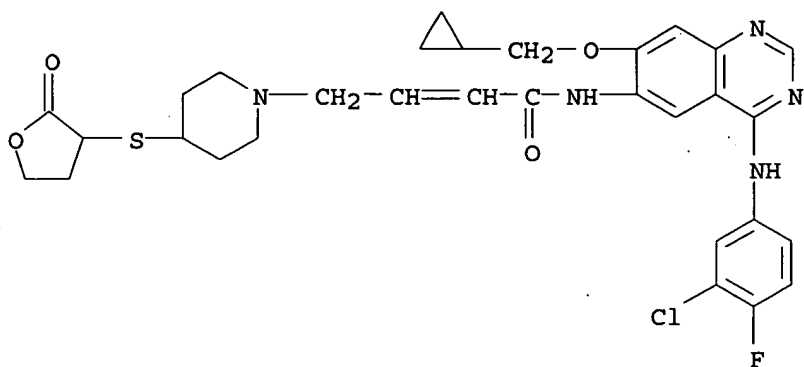
RN 365532-47-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-1-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)



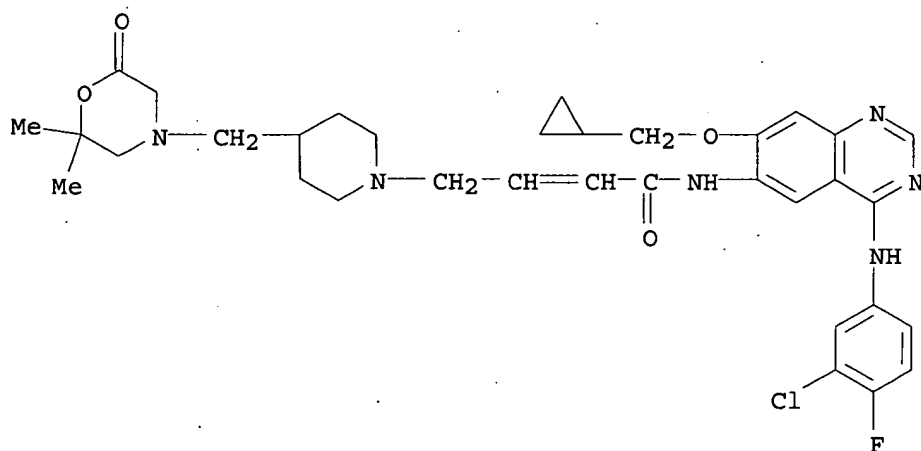
RN 365532-48-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(4-[(tetrahydro-2-oxo-3-furanyl)thio]-1-piperidinyl)]-6-quinazolinyl-(9CI) (CA INDEX NAME)



RN 365532-49-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)



IT 290303-47-8P 290304-01-7P 365532-06-5P

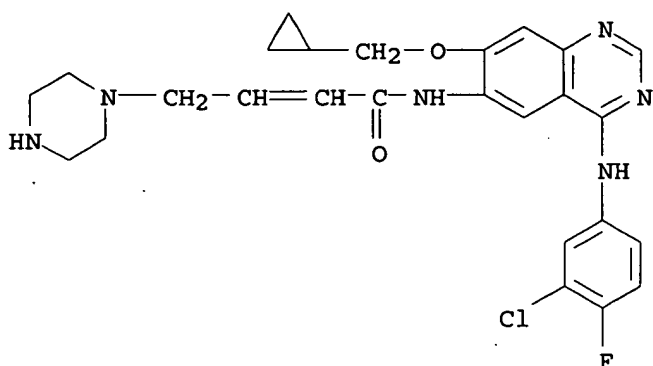
365532-10-1P 365532-18-9P 365532-21-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

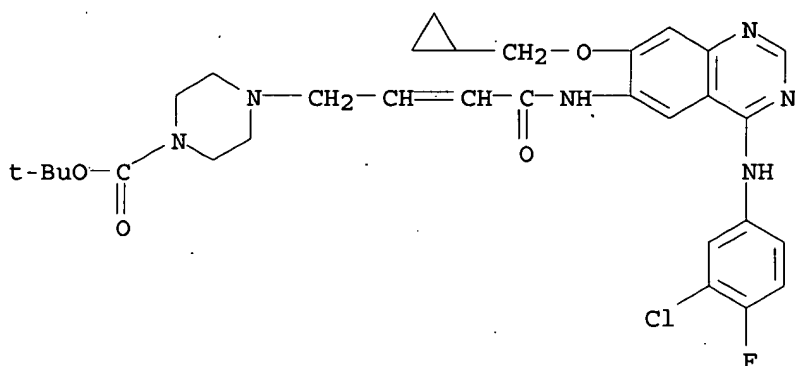
RN 290303-47-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)



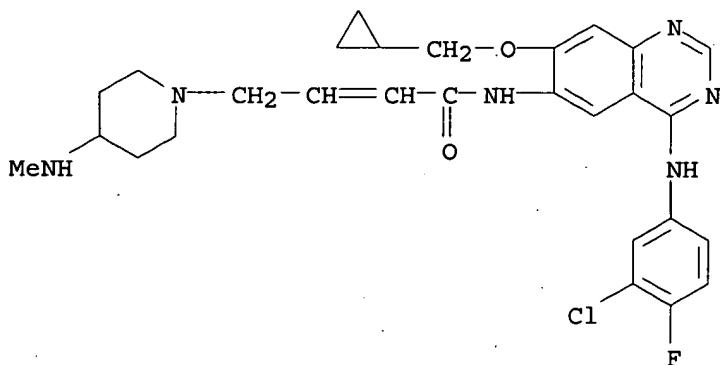
RN 290304-01-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



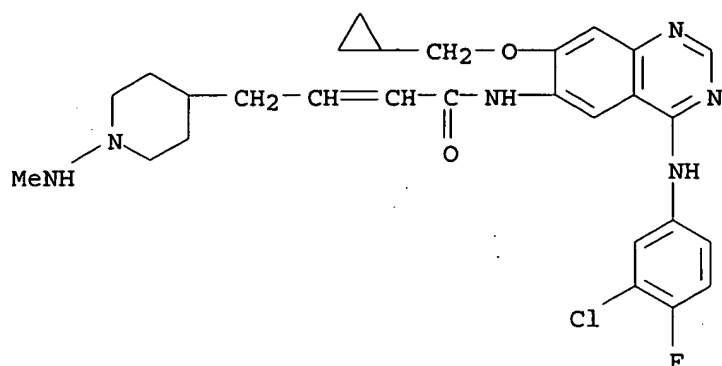
RN 365532-06-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(methylamino)-1-piperidiny]- (9CI) (CA INDEX NAME)



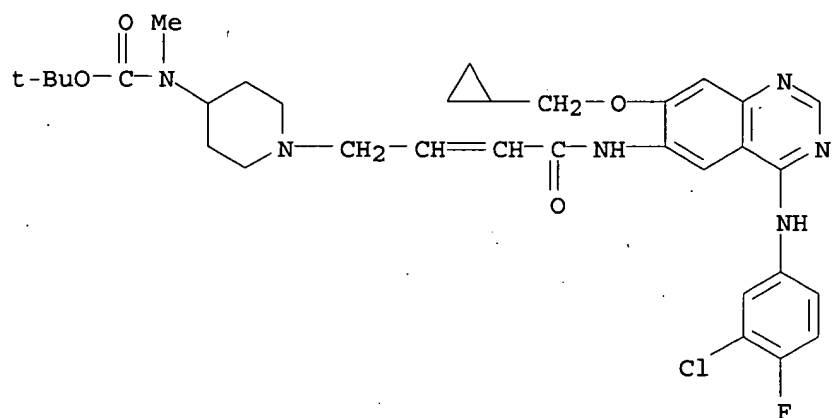
RN 365532-10-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[1-(methylamino)-4-piperidiny]- (9CI) (CA INDEX NAME)



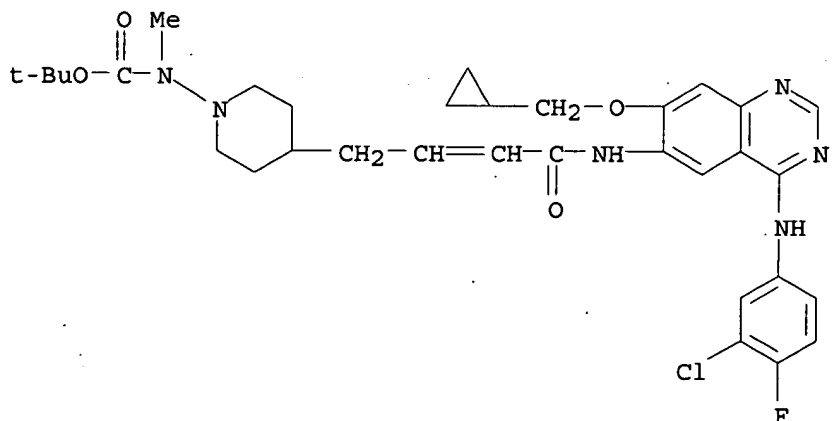
RN 365532-18-9 CAPLUS

CN Carbamic acid, [1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 365532-21-4 CAPLUS

CN Carbamic acid, [4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 365532-36-1P 365532-37-2P 365532-38-3P

365532-41-8P 365532-43-0P 365532-44-1P
365532-46-3P

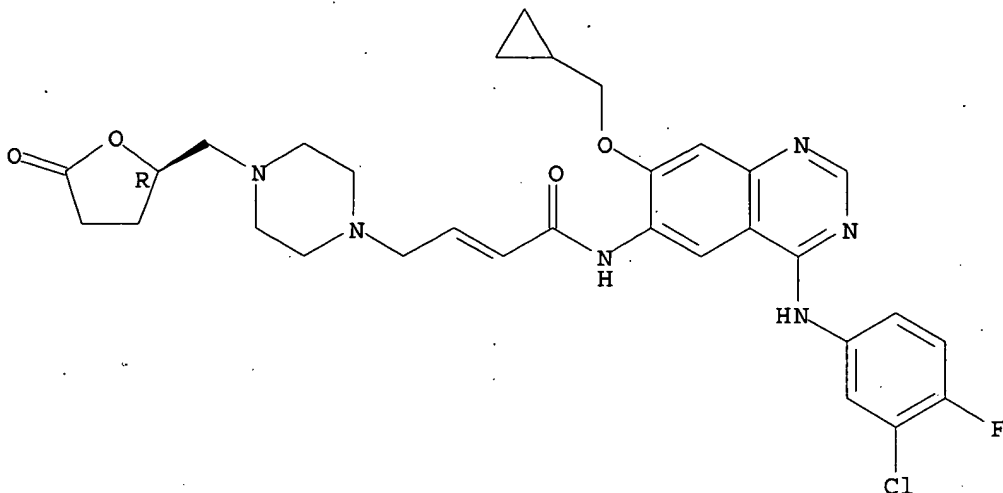
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

RN 365532-36-1 CAPLUS

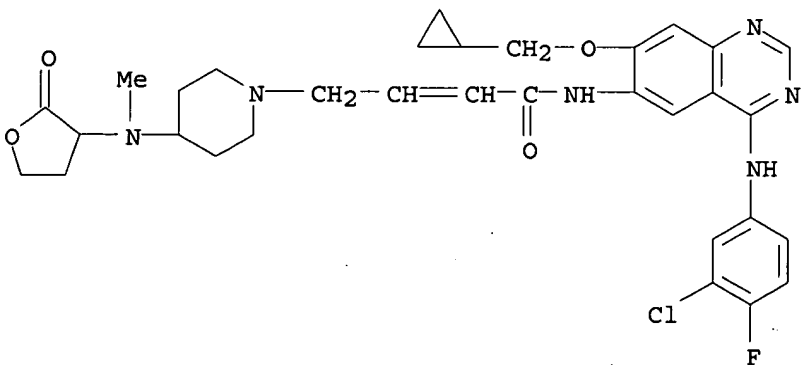
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2R)-tetrahydro-5-oxo-2-furanyl)methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 365532-37-2 CAPLUS

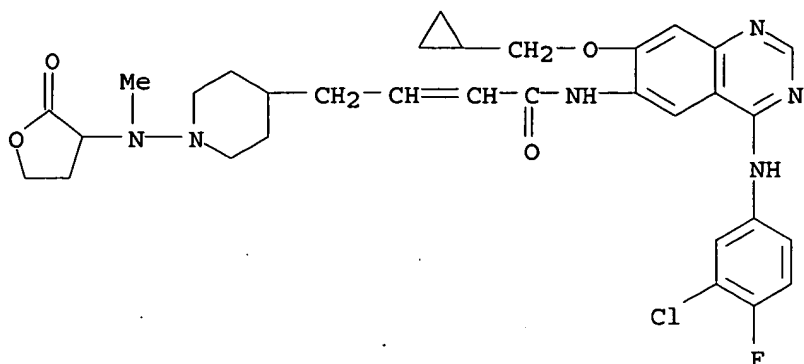
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 365532-38-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[1-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-4-piperidinyl]- (9CI) (CA INDEX NAME)

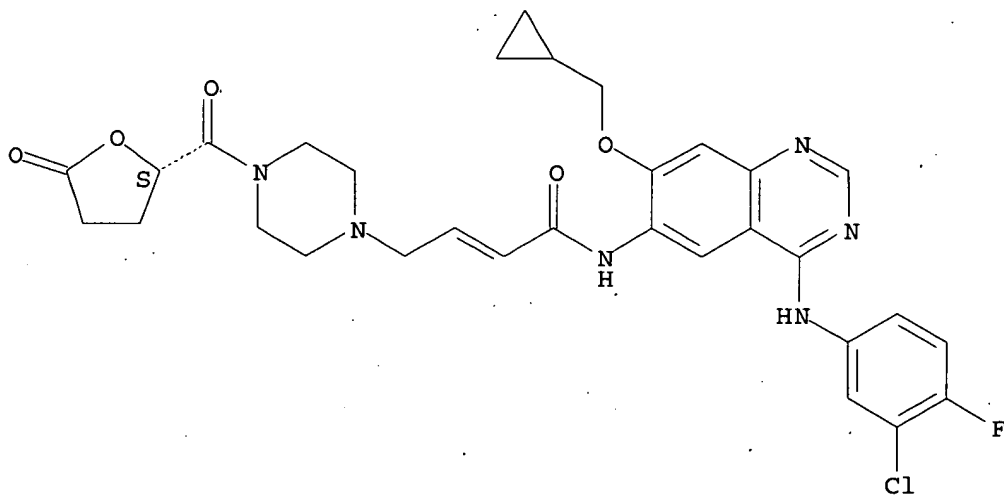
10/ 023,099



RN 365532-41-8 CAPLUS

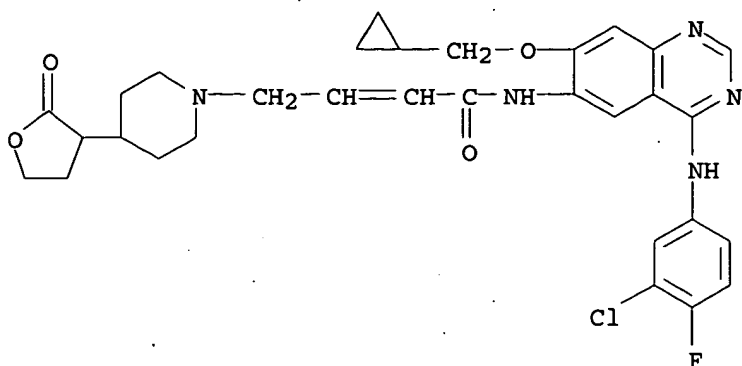
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



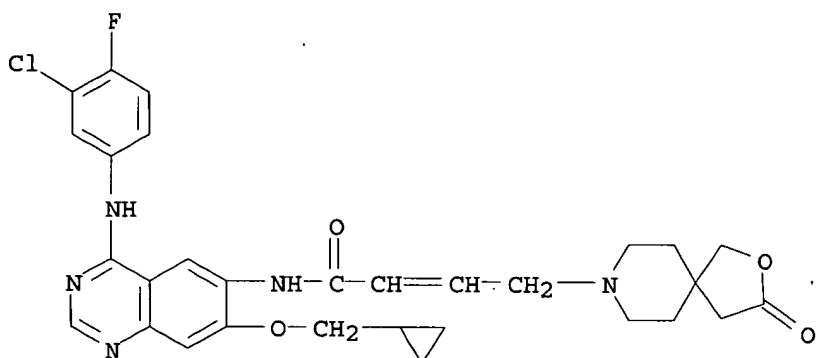
RN 365532-43-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)



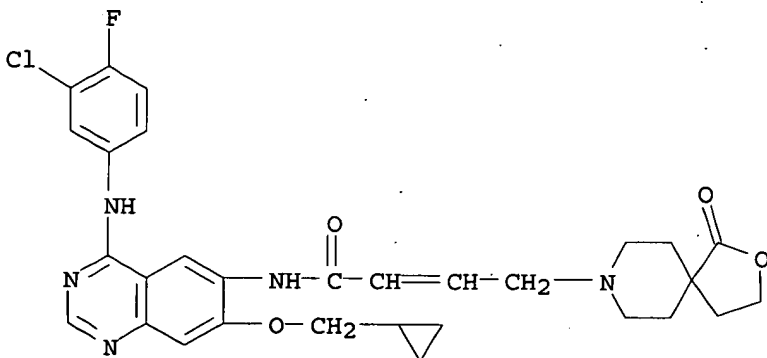
RN 365532-44-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(3-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)-(9CI) (CA INDEX NAME)



RN 365532-46-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)-(9CI) (CA INDEX NAME)



L3 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:514231 CAPLUS

DOCUMENT NUMBER: 135:251424

TITLE: 6-Substituted-4-(3-bromophenylamino)quinazolines as

Putative Irreversible Inhibitors of the Epidermal Growth Factor Receptor (EGFR) and Human Epidermal Growth Factor Receptor (HER-2) Tyrosine Kinases with Enhanced Antitumor Activity

AUTHOR(S): Tsou, Hwei-Ru; Mamuya, Nellie; Johnson, Bernard D.; Reich, Marvin F.; Gruber, Brian C.; Ye, Fei; Nilakantan, Ramaswamy; Shen, Ru; Discafani, Carolyn; DeBlanc, Ronald; Davis, Rachel; Koehn, Frank E.; Greenberger, Lee M.; Wang, Yu-Fen; Wissner, Allan

CORPORATE SOURCE: Wyeth-Ayerst Research A Division of American Home Products, Pearl River, NY, 10965-1215, USA

SOURCE: Journal of Medicinal Chemistry (2001), 44(17), 2719-2734

CODEN: JMCMAR; ISSN: 0022-2623

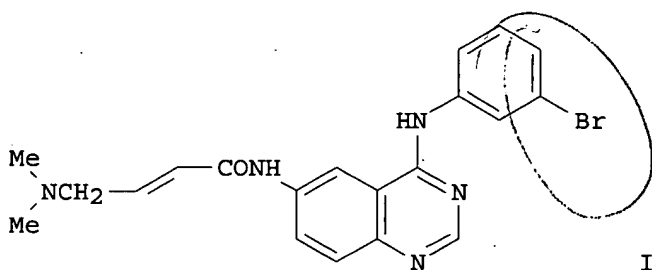
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:251424

GI



not claimed

AB A series of new 6-substituted-4-(3-bromophenylamino)quinazoline derivs. that may function as irreversible inhibitors of epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor (HER-2) tyrosine kinases have been prepd. These inhibitors have, at the C-6 position, butynamide, crotonamide, and methacrylamide Michael acceptors bearing water-solubilizing substituents. These compds. were prepd. by acylation of 6-amino-4-(3-bromophenylamino)quinazoline with unsatd. acid chlorides or mixed anhydrides. We show that attaching a basic functional group onto the Michael acceptor results in greater reactivity, due to intramol. catalysis of the Michael addn. and/or an inductive effect of the protonated basic group. This, along with improved water soly., results in compds. with enhanced biol. properties. We present mol. modeling and exptl. evidence that these inhibitors interact covalently with the target enzymes. One compd., (I) was shown to have excellent oral activity in a human epidermoid carcinoma (A431) xenograft model in nude mice.

IT 361392-73-6P 361392-74-7P 361392-75-8P
361392-76-9P 361392-77-0P 361392-78-1P
361392-79-2P 361392-80-5P 361392-81-6P
361392-82-7P 361392-83-8P 361392-89-4P
361392-90-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

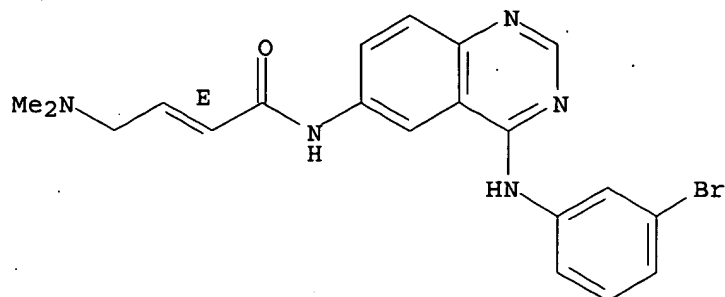
(prepn. and structure activity relations of antitumor (bromophenylamino)quinazolines as putative irreversible inhibitors of EGFR and human epidermal growth factor receptor (HER-2) tyrosine kinase)

RN 361392-73-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)-, (2E)- (9CI) (CA INDEX NAME)

10/ 023,099

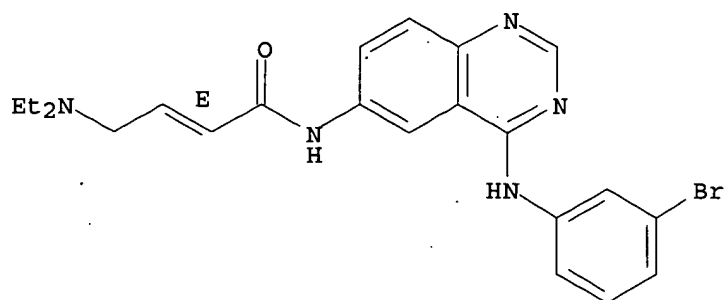
Double bond geometry as shown.



RN 361392-74-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(diethylamino)-, (2E)-(9CI) (CA INDEX NAME)

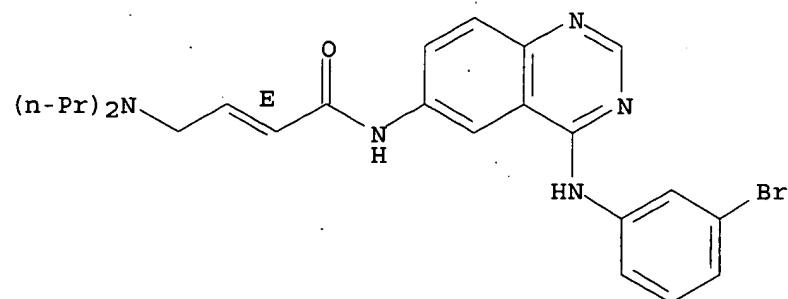
Double bond geometry as shown.



RN 361392-75-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dipropylamino)-, (2E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

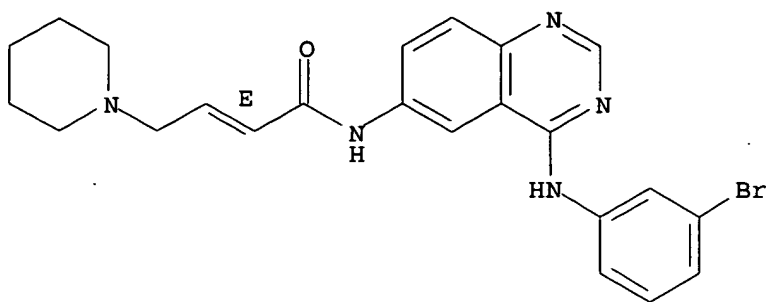


RN 361392-76-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(1-piperidiny)-, (2E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

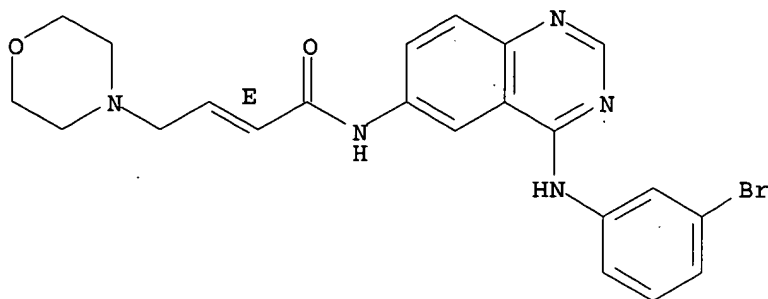
10/ 023,099



RN 361392-77-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(4-morpholinyl)-, (2E)- (9CI) (CA INDEX NAME)

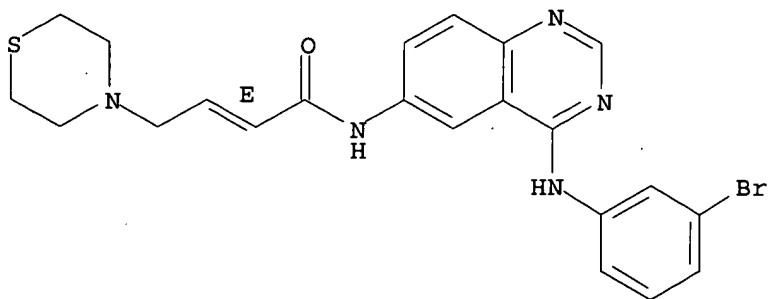
Double bond geometry as shown.



RN 361392-78-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(4-thiomorpholinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



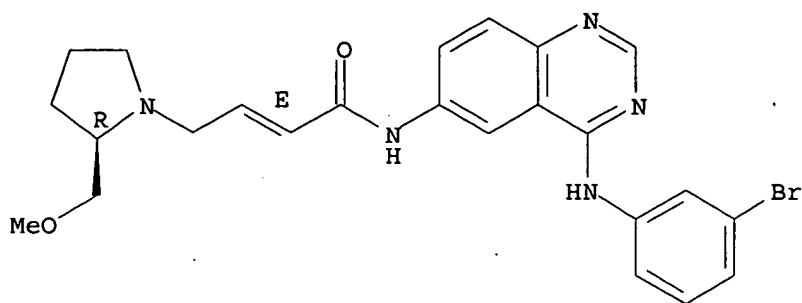
RN 361392-79-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

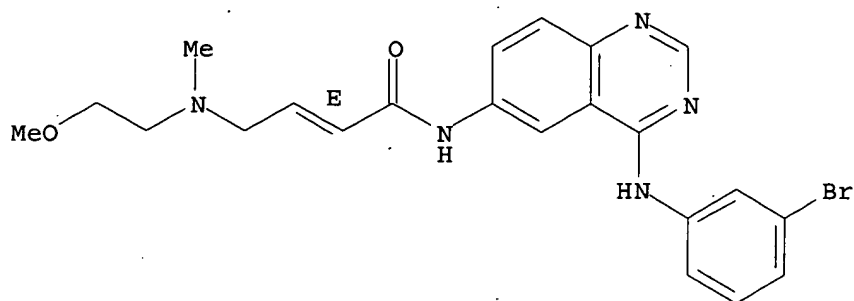
10/ 023,099



RN 361392-80-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]-, (2E)- (9CI) (CA INDEX NAME)

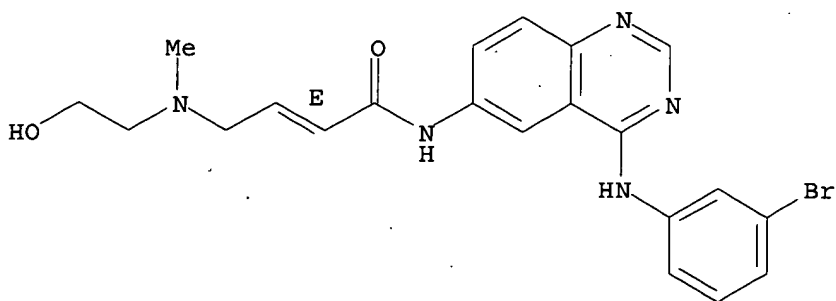
Double bond geometry as shown.



RN 361392-81-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2-hydroxyethyl)methylamino]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

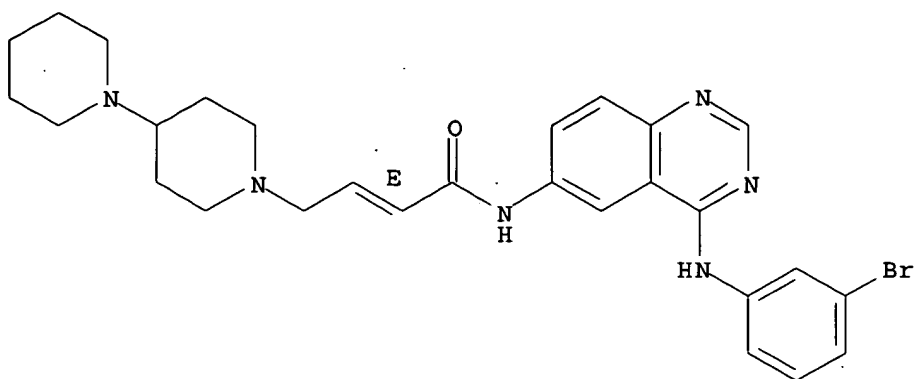


RN 361392-82-7 CAPLUS

CN 2-Butenamide, 4-[1,4'-bipiperidin]-1'-yl-N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

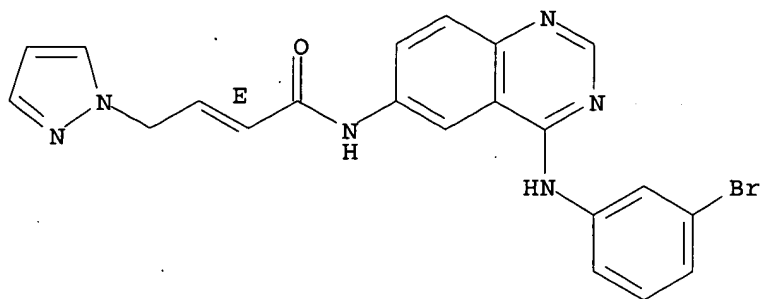
10/ 023,099



RN 361392-83-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(1H-pyrazol-1-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

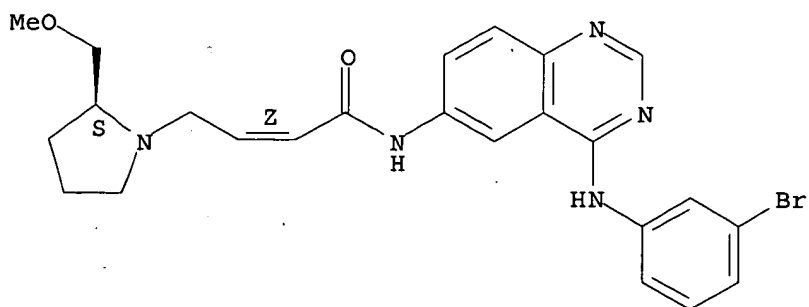


RN 361392-89-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]-, (2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

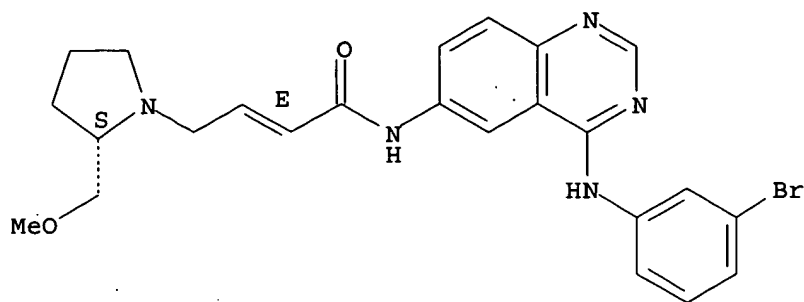


RN 361392-90-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:185 CAPLUS

DOCUMENT NUMBER: 134:207783

TITLE: Tyrosine kinase inhibitors. 18. 6-Substituted 4-anilinoquinazolines and 4-anilinopyrido[3,4-d]pyrimidines as soluble, irreversible inhibitors of the epidermal growth factor receptor

AUTHOR(S): Smaill, Jeff B.; Showalter, H. D. Hollis; Zhou, Hairong; Bridges, Alexander J.; McNamara, Dennis J.; Fry, David W.; Nelson, James M.; Sherwood, Veronika; Vincent, Patrick W.; Roberts, Bill J.; Elliott, William L.; Denny, William A.

CORPORATE SOURCE: Auckland Cancer Society Research Centre Faculty of Medicine and Health Science, The University of Auckland, Auckland, 92019, N. Z.

SOURCE: Journal of Medicinal Chemistry (2001), 44(3), 429-440
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 4-Anilinoquinazoline- and 4-anilinopyrido[3,4-d]pyrimidine-6'-acrylamides are potent pan-erbB tyrosine kinase inactivators, and one example (CI-1033) is in clin. trial. A series of analogs with a variety of Michael acceptor units at the 6-position, I [X = N, C, R1 = H, Me, (CH2)2NMe2, etc., R2 = H, Me, R3 = H, cis-Cl, CF3, etc.], II, and III (X = N, C, R1 = NHSO2CH:CH2, SO2CH2CH2OH, SO2CH:CH2, SOCH:CH2), were prepd. to define the structural requirements for irreversible inhibition. A particular goal was to det. whether addnl. functions to increase soly. could be appended to the Michael acceptor. Substituted acrylamides were prepd. by direct acylation of the corresponding 6-amines with the requisite acid or acid chloride. Vinylsulfonamide derivs. were obtained by acylation of the amines with chloroethylsulfonyl chloride followed by base-promoted elimination. Vinylsulfone and vinylsulfine derivs. were prepd. by oxidn. and base elimination of a hydroxyethylthio intermediate. The compds. were evaluated for their inhibition of phosphorylation of the isolated EGFR enzyme and for inhibition of EGF-stimulated autophosphorylation of EGFR in A431 cells and of heregulin-stimulated autophosphorylation of erbB2 in MDA-MB 453 cells. Substitution at the nitrogen of the acrylamide was tolerated only with a Me group; larger

substituents were dystherapeutic, and no substitution at all was tolerated at the acrylamide .alpha.-carbon. In contrast, while electron-donating groups at the acrylamide .beta.-carbon were not useful, even quite large electron-withdrawing groups (which increase its electrophilicity) were tolerated. A series of derivs. with soly.-enhancing substituents linked to the acrylamide .beta.-carbon via amides were potent irreversible inhibitors of isolated EGFR (IC50s = 0.4-1.1 nM), with weakly basic morpholine and imidazole derivs. being the best. Vinylsulfonamides were also potent and irreversible inhibitors, but vinylsulfones and vinylsulfines were reversible and only poorly active. Two compds. were evaluated against A431, H125, and MCF-7 xenografts in nude mice but were inferior in these assays to the clin. trial compd. CI-1033.

IT 198960-34-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn., epidermal growth factor receptor inhibitory activity, and structure-activity relationship of anilinoquinazolines and -pyridopyrimidines)

RN 198960-34-8 CAPLUS

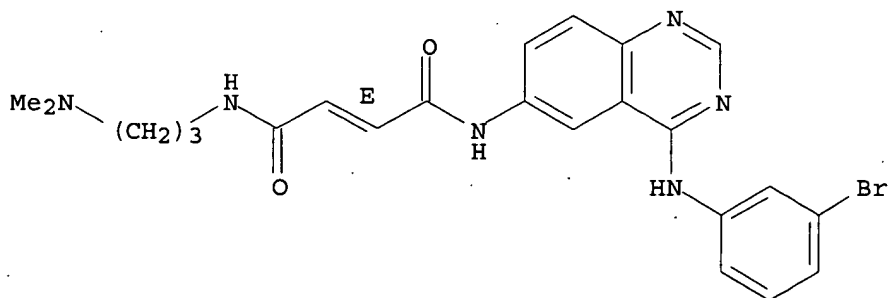
CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]-, (2E)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 198960-33-7

CMF C23 H25 Br N6 O2

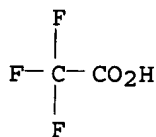
Double bond geometry as shown.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



REFERENCE COUNT:

24

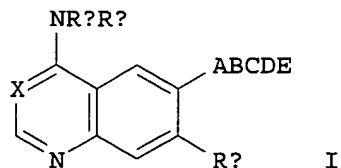
THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/ 023,099

DOCUMENT NUMBER: 134:71599
 TITLE: Preparation of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors.
 INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Metz, Thomas; Solca, Flavio; Jung, Birgit; Baum, Anke
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: PCT Int. Appl., 104 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078735	A1	20001228	WO 2000-EP5547	20000616
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19928281	A1	20001228	DE 1999-19928281	19990621
DE 10023085	A1	20011115	DE 2000-10023085	20000511
BR 2000011834	A	20020312	BR 2000-11834	20000616
EP 1194418	A1	20020410	EP 2000-936888	20000616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003502410	T2	20030121	JP 2001-504901	20000616
EE 200100695	A	20030217	EE 2001-695	20000616
BG 106189	A	20020830	BG 2001-106189	20011207
US 2002169180	A1	20021114	US 2001-16280	20011210
NO 2001006185	A	20011218	NO 2001-6185	20011218
PRIORITY APPLN. INFO::				
			DE 1999-19928281 A	19990621
			US 1999-146644P P	19990730
			DE 2000-10023085 A	20000511
			WO 2000-EP5547 W	20000616

OTHER SOURCE(S): MARPAT 134:71599
 GI



AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH₂, PhCH₂CH₂; Rc = (substituted) cycloalkoxy, cycloalkylalkoxy; A = (alkyl-substituted) imino; B = CO, SO₂; C = (substituted) allenylene, vinylene, butadienylene, ethynylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, carbonyloxyalkylene, carbonyliminoalkylene, bond, etc.; E = amino, (substituted) alkylamino, dialkylamino, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propoxy]quinazoline (prepn. given) in CH₂Cl₂ contg. Et₃N at -10.degree. was treated with acryloyl chloride in THF to give 35% 4-[(3-

bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation of F/L HERC cells with $IC_{50} = <0.35$ nM.

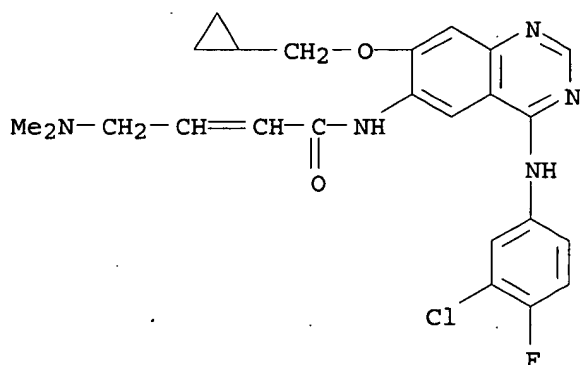
IT 314771-10-3P 314771-12-5P 314771-31-8P
 314771-32-9P 314771-33-0P 314771-34-1P
 314771-35-2P 314771-36-3P 314771-37-4P
 314771-38-5P 314771-45-4P 314771-46-5P
 314771-47-6P 314771-48-7P 314771-49-8P
 314771-50-1P 314771-51-2P 314771-52-3P
 314771-53-4P 314771-54-5P 314771-55-6P
 314771-56-7P 314771-57-8P 314771-58-9P
 314771-59-0P 314771-60-3P 314771-61-4P
 314771-62-5P 314771-63-6P 314771-64-7P
 314771-65-8P 314771-66-9P 314771-67-0P
 314771-68-1P 314771-69-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors)

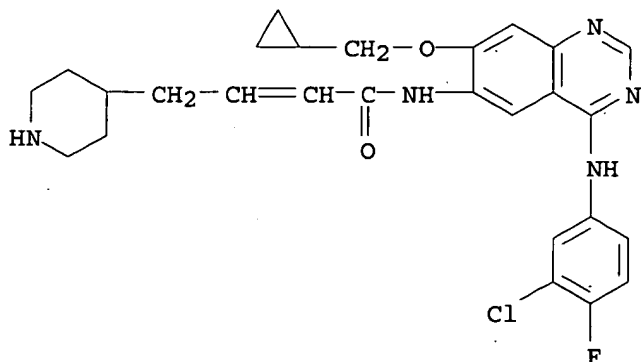
RN 314771-10-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



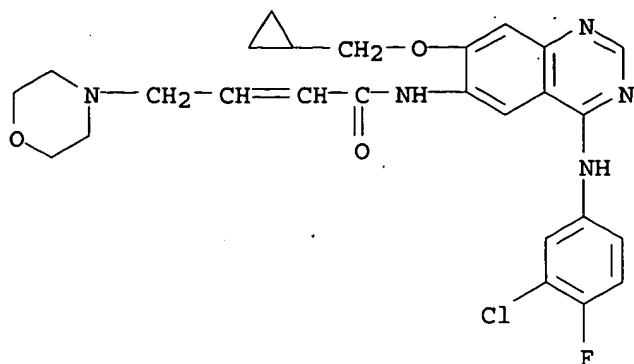
RN 314771-12-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)



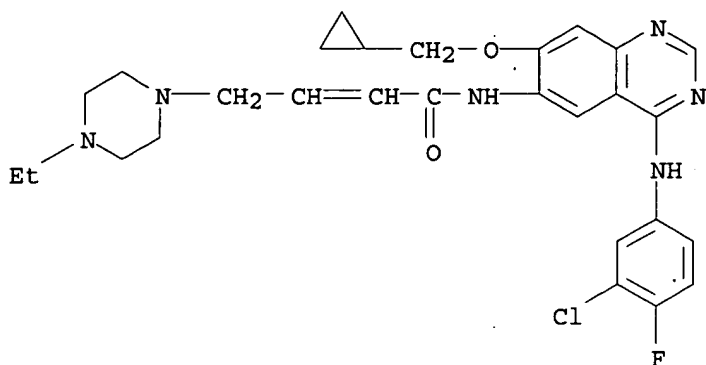
RN 314771-31-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)



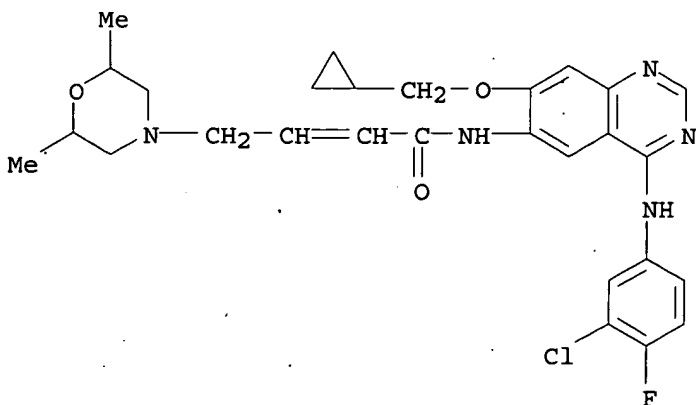
RN 314771-32-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-ethyl-1-piperazinyl) - (9CI) (CA INDEX NAME)



RN 314771-33-0 CAPLUS

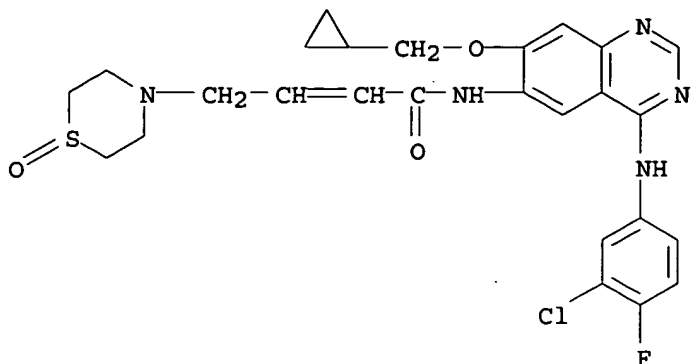
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,6-dimethyl-4-morpholinyl) - (9CI) (CA INDEX NAME)



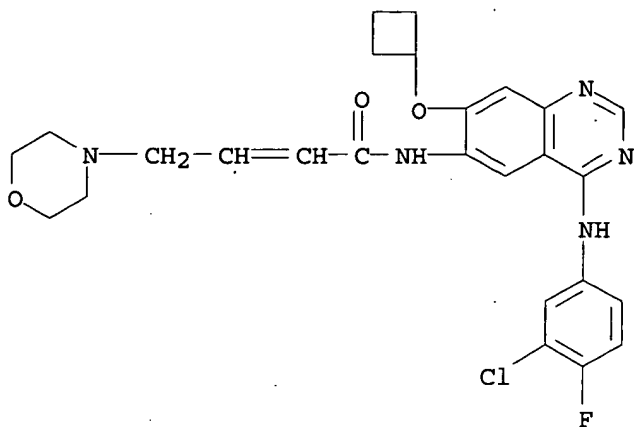
RN 314771-34-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxido-4-thiomorpholinyl) - (9CI) (CA INDEX NAME)

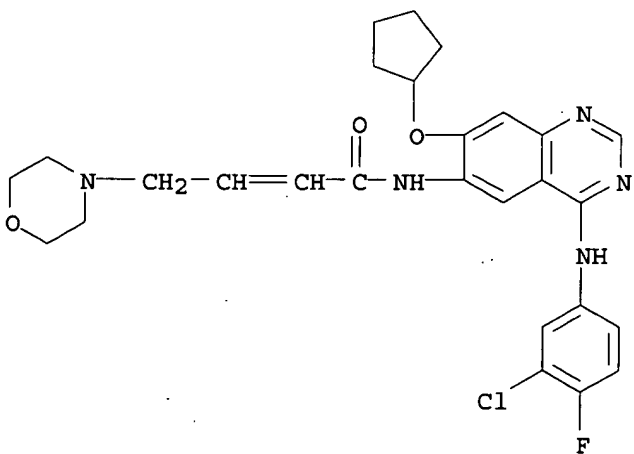
10/ 023,099



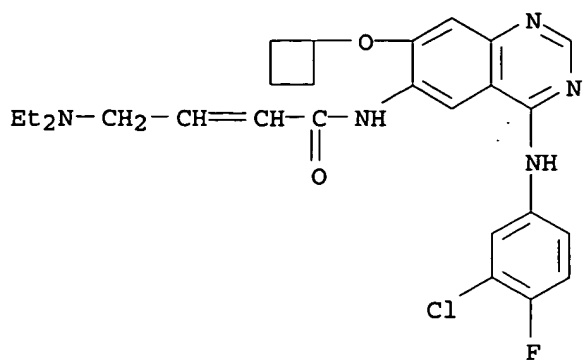
RN 314771-35-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(4-morpholinyl) - (9CI) (CA INDEX NAME)



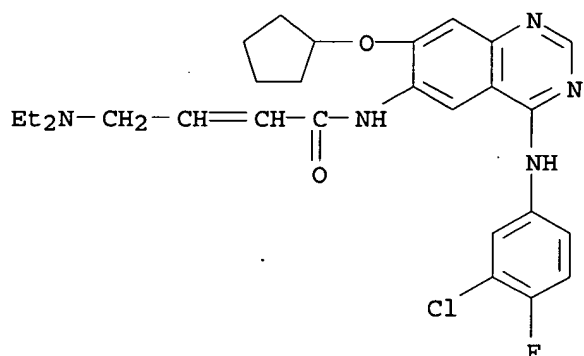
RN 314771-36-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(4-morpholinyl) - (9CI) (CA INDEX NAME)



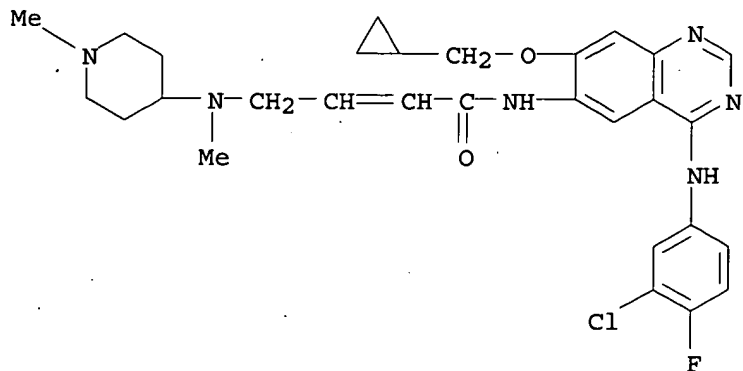
RN 314771-37-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(diethylamino) - (9CI) (CA INDEX NAME)



RN 314771-38-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



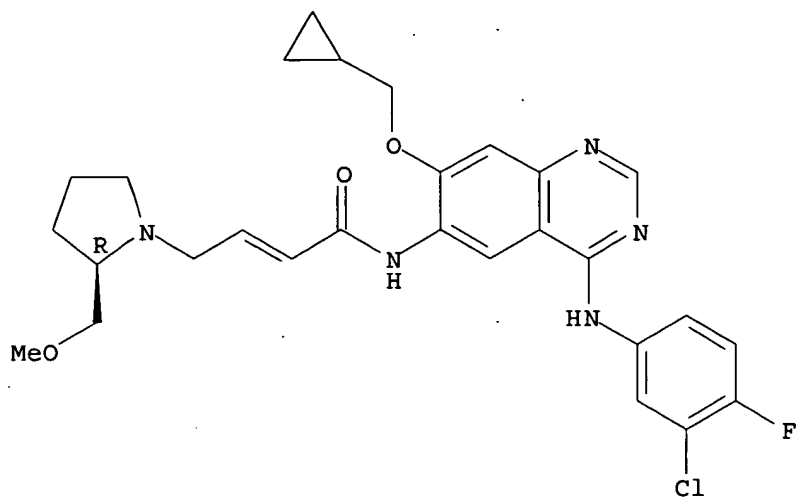
RN 314771-45-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(1-methyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)



RN 314771-46-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

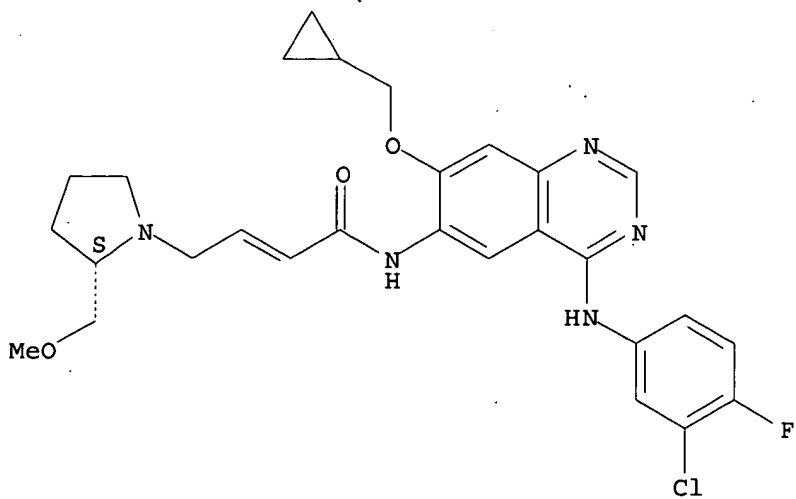
10/ 023,099

Absolute stereochemistry.
Double bond geometry unknown.

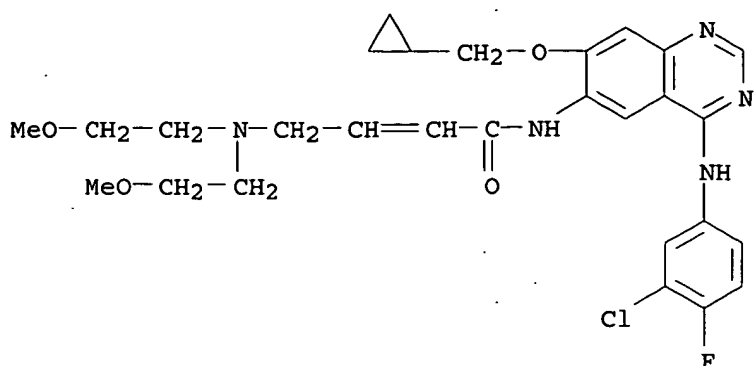


RN 314771-47-6 CAPLUS
CN 2-Butenamide, N- [4- [(3-chloro-4-fluorophenyl)amino] -7- (cyclopropylmethoxy) -
6-quinazolinyl] -4- [(2S) -2- (methoxymethyl) -1-pyrrolidinyl] - (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

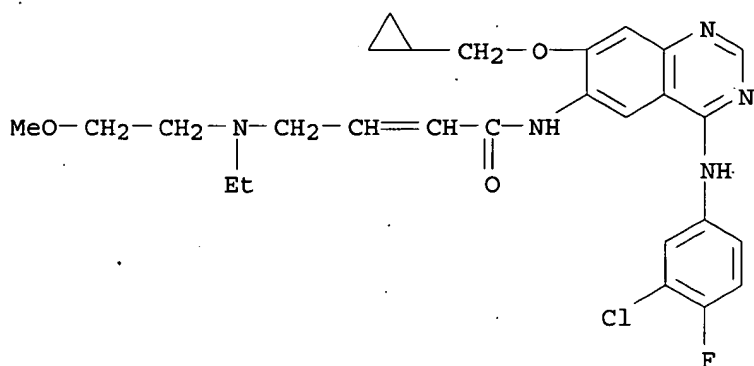


RN 314771-48-7 CAPLUS
CN 2-Butenamide, 4- [bis (2-methoxyethyl) amino] -N- [4- [(3-chloro-4-
fluorophenyl)amino] -7- (cyclopropylmethoxy) -6-quinazolinyl] - (9CI) (CA
INDEX NAME)



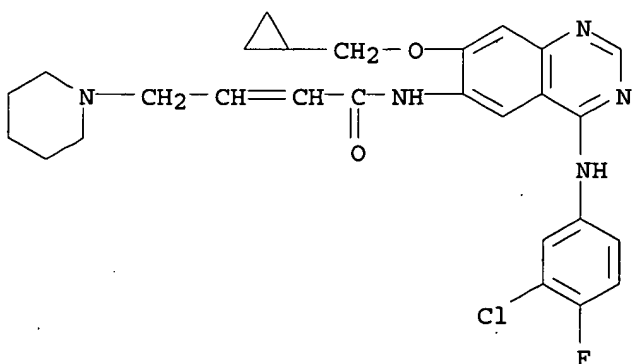
RN 314771-49-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]-(9CI) (CA INDEX NAME)



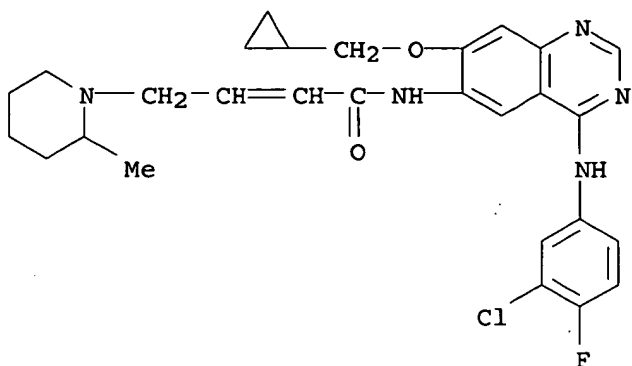
RN 314771-50-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperidinyl)-(9CI) (CA INDEX NAME)



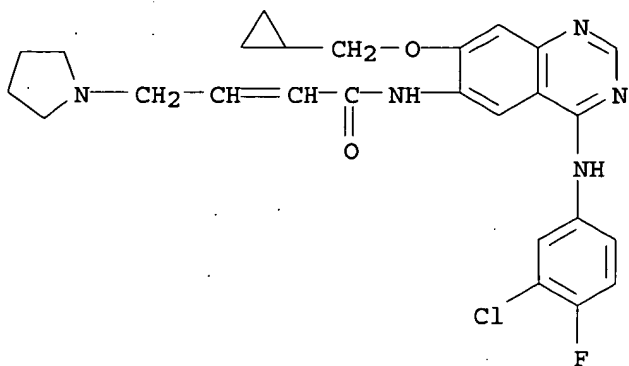
RN 314771-51-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-methyl-1-piperidinyl)-(9CI) (CA INDEX NAME)



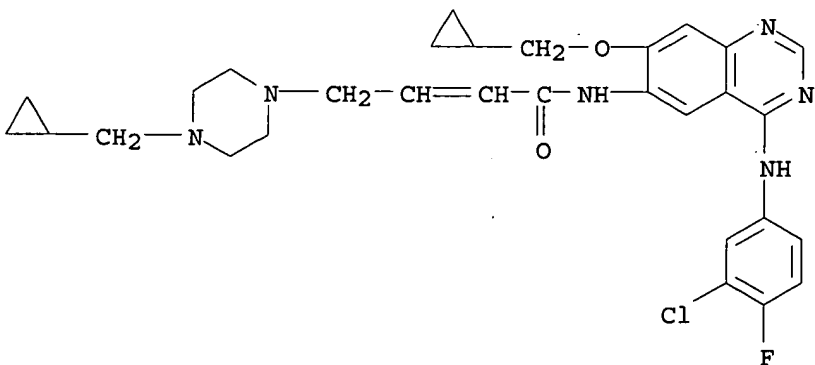
RN 314771-52-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 314771-53-4 CAPLUS

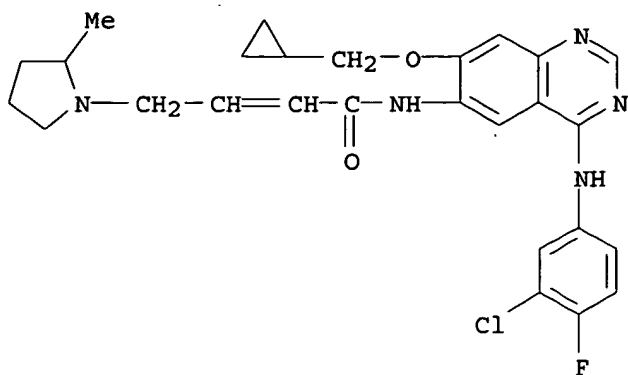
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(cyclopropylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 314771-54-5 CAPLUS

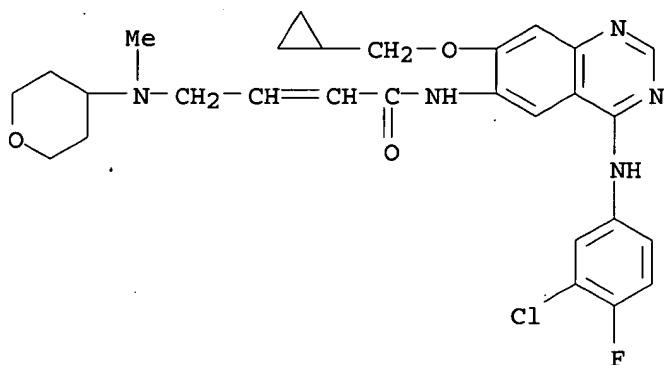
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-methyl-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

10/ 023,099



RN 314771-55-6 CAPLUS

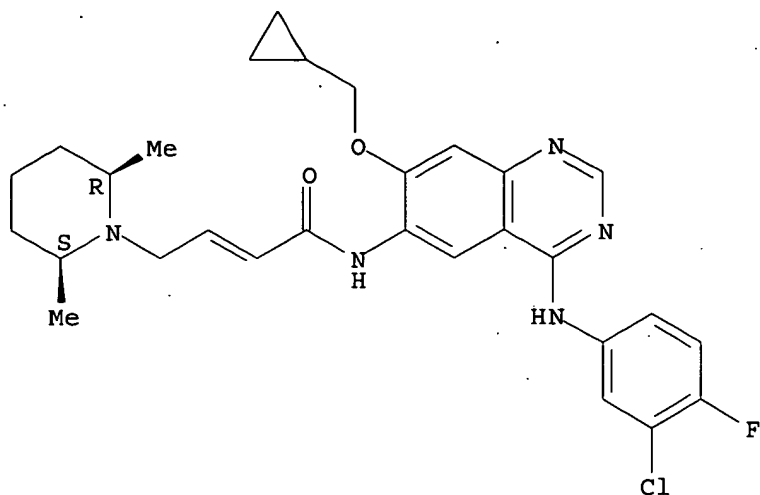
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)



RN 314771-56-7 CAPLUS

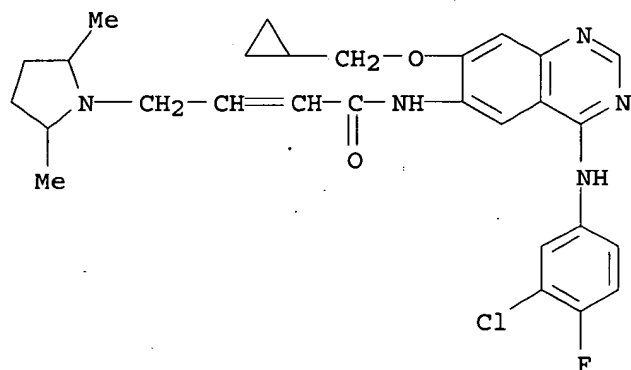
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R,6S)-2,6-dimethyl-1-piperidinyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.



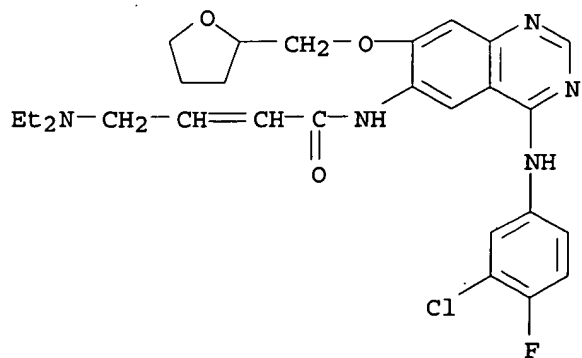
RN 314771-57-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,5-dimethyl-1-pyrrolidinyl) - (9CI) (CA INDEX NAME)



RN 314771-58-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(diethylamino) - (9CI) (CA INDEX NAME)



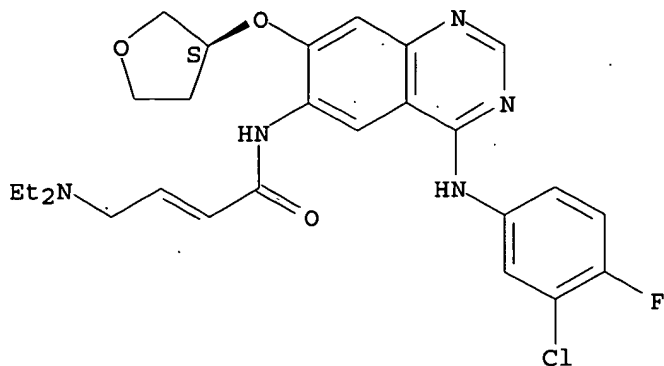
RN 314771-59-0 CAPLUS

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10/ 023,099

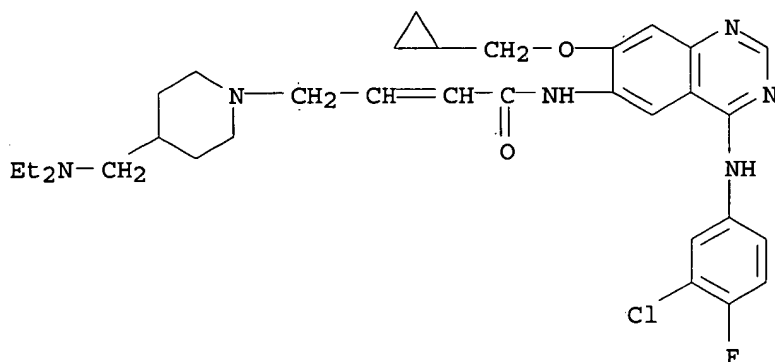
furanyloxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



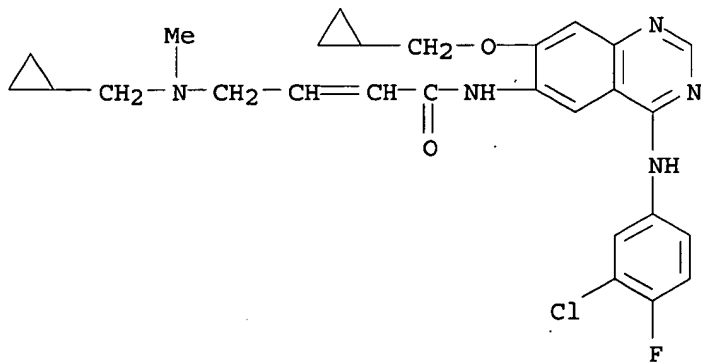
RN 314771-60-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(diethylamino)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 314771-61-4 CAPLUS

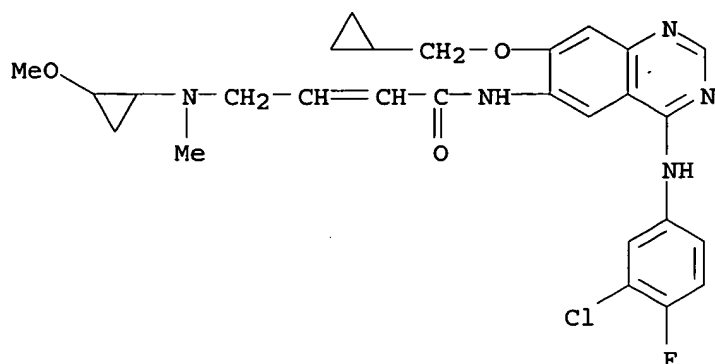
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(cyclopropylmethyl)methylamino]- (9CI) (CA INDEX NAME)



RN 314771-62-5 CAPLUS

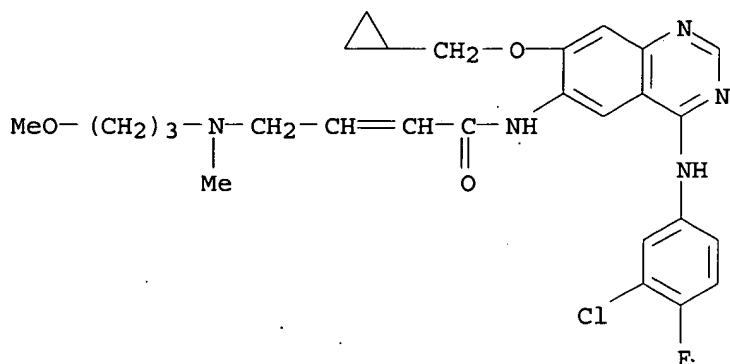
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6-quinazolinyl]-4-[(2-methoxycyclopropyl)methylamino] - (9CI) (CA INDEX NAME)



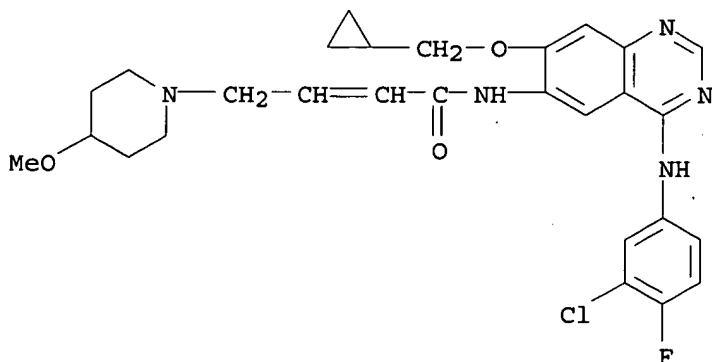
RN 314771-63-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3-methoxypropyl)methylamino] - (9CI) (CA INDEX NAME)



RN 314771-64-7 CAPLUS

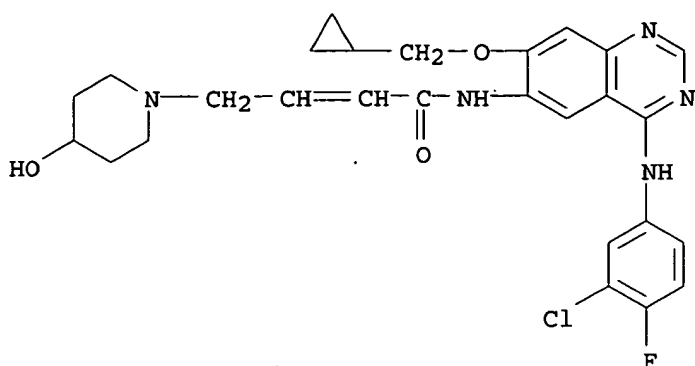
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-methoxy-1-piperidinyl) - (9CI) (CA INDEX NAME)



RN 314771-65-8 CAPLUS

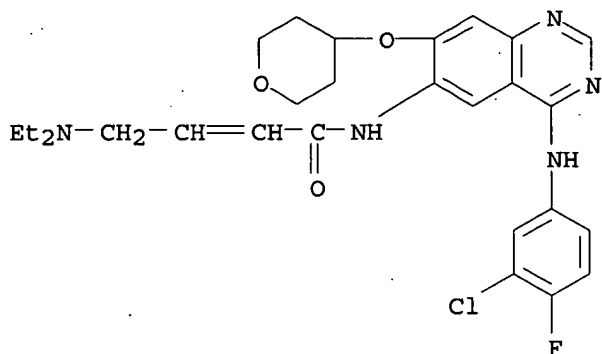
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-hydroxy-1-piperidinyl) - (9CI) (CA INDEX NAME)

10/ 023,099



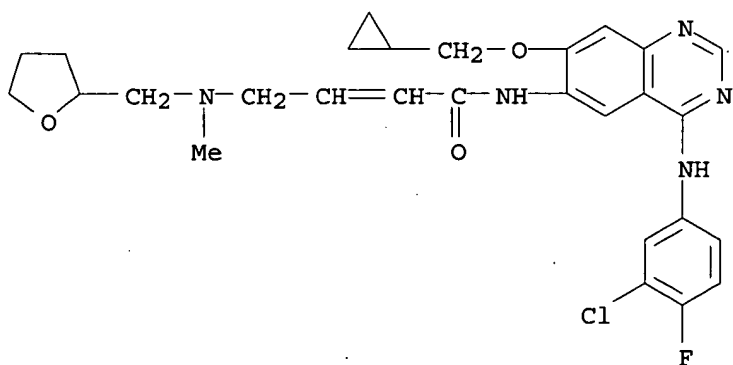
RN 314771-66-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



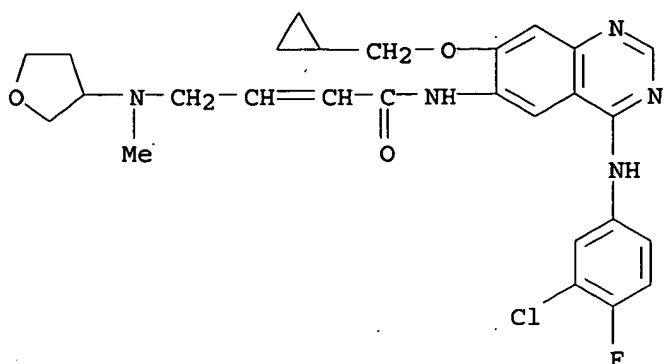
RN 314771-67-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



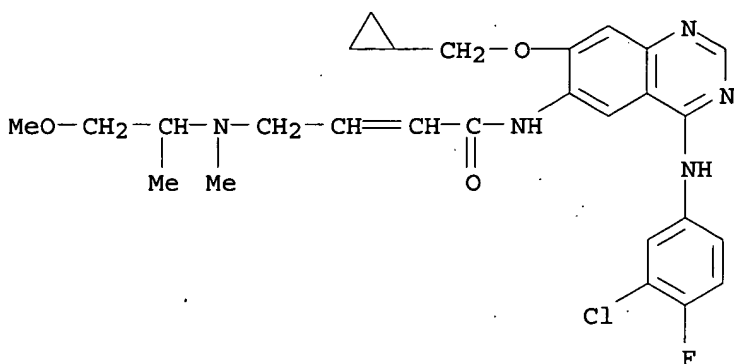
RN 314771-68-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-3-furanyl)amino]- (9CI) (CA INDEX NAME)



RN 314771-69-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxy-1-methylethyl)methylamino]-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:628125 CAPLUS

DOCUMENT NUMBER: 133:207919

TITLE: Preparation of 4-amino-quinazoline and quinoline derivatives having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas; Solca, Flavio; Blech, Stefan

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 232 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051991	A1	20000908	WO 2000-EP1496	20000224
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,				

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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DE 19911366	A1	20000921	DE 1999-19911366	19990315
DE 19928306	A1	20001228	DE 1999-19928306	19990621
DE 19954816	A1	20010517	DE 1999-19954816	19991113
CA 2361174	AA	20000908	CA 2000-2361174	20000224
EP 1157011	A1	20011128	EP 2000-910695	20000224

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

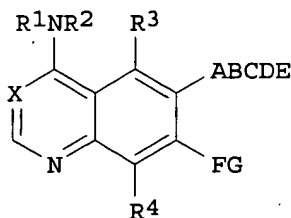
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JP 2002538145	T2	20021112	JP 2000-602218	20000224
EE 200100449	A	20021216	EE 2001-449	20000224
BG 105765	A	20020329	BG 2001-105765	20010801
HR 20010617	A1	20021031	HR 2001-617	20010823
NO 2001004114	A	20011015	NO 2001-4114	20010824

PRIORITY APPLN. INFO.:

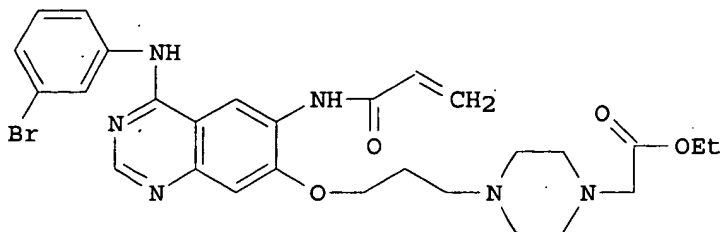
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DE 1999-19911366	A	19990315
DE 1999-19928306	A	19990621
US 1999-149329P	P	19990817
DE 1999-19954816	A	19991113
WO 2000-EP1496	W	20000224

OTHER SOURCE(S):
GI

MARPAT 133:207919



I



II

AB Title compds. [I; R1 = H, C1-C4-alkyl; R2 = (un)substituted Ph, benzyl, 1-phenylethyl; R3, R4 independently = H, F, Cl, CH3O, CH3OCH2, (CH3)2NCH2, (CH3CH2)2NCH2, pyrrolidino, piperidino, morpholino; X = C(CN), N; A = O, NH, (C1-C4)-alkylN; B = CO, SO2; C = 1,3-allenylene, 1,1-vinylene, 1,2-vinylene, 1,3-butadien-1,4-ylene, with CH3, CF3 substitution; D =

alkylene, CO-alkylene, SO₂-alkylene; CO, SO₂; E = HOCO(CH₂)_nNR₅, (HO)2P(:O)(CH₂)_nNR₅; n = 1-6; R₅ = H, alkyl], tautomers, stereoisomers, and physiol. acceptable salts are prepd. and having valuable pharmacol. properties, particularly an inhibiting effect on signal transduction mediated by tyrosine kinases. Title compds. are useful for treating tumoral diseases, diseases of the lungs and respiratory tract. Thus, the title compd. II was prepd. and tested by Cell Titer 96TM Aq.

Nonradioactive Cell Proliferation Assay.

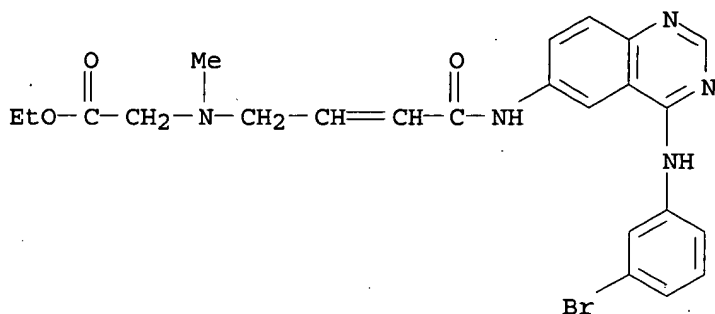
IT 289700-68-1P 290301-75-6P 290301-88-1P
290301-94-9P 290301-96-1P 290302-11-3P
290302-19-1P 290302-25-9P 290302-33-9P
290302-39-5P 290302-47-5P 290302-98-6P
290303-04-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

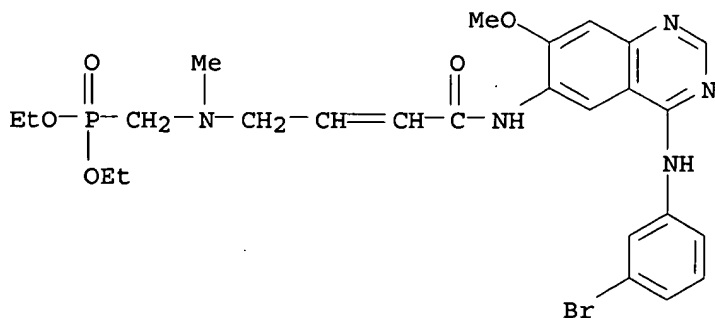
RN 289700-68-1 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 290301-75-6 CAPLUS

CN Phosphonic acid, [[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



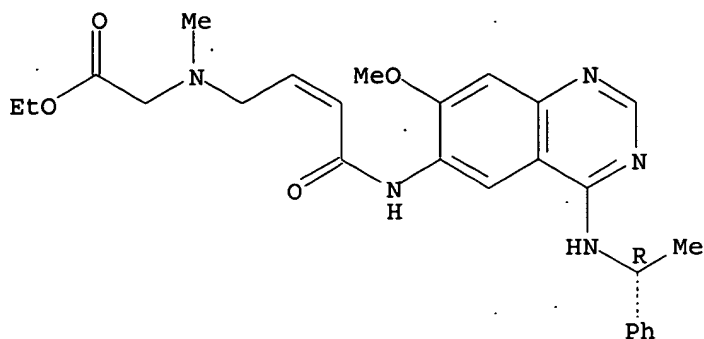
RN 290301-88-1 CAPLUS

CN Glycine, N-[4-[[7-methoxy-4-[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

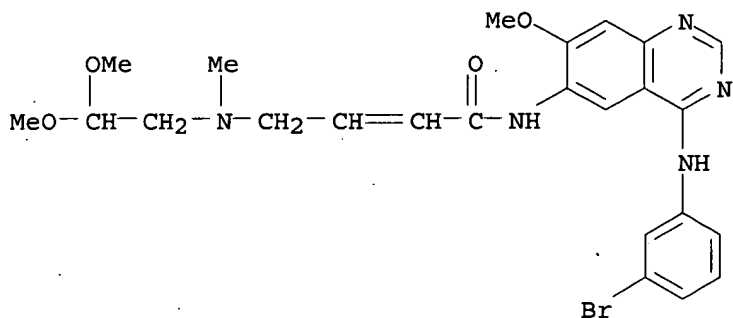
10/ 023,099

Double bond geometry unknown.



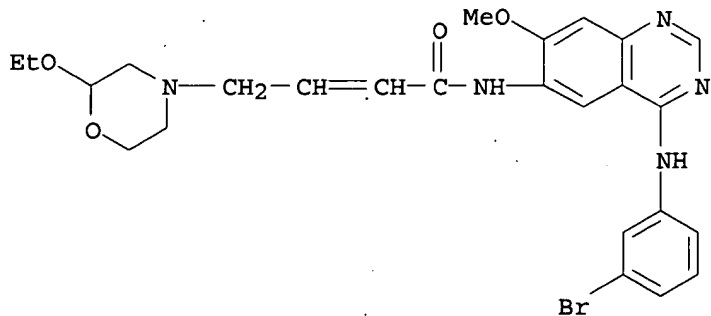
RN 290301-94-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(2,2-dimethoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



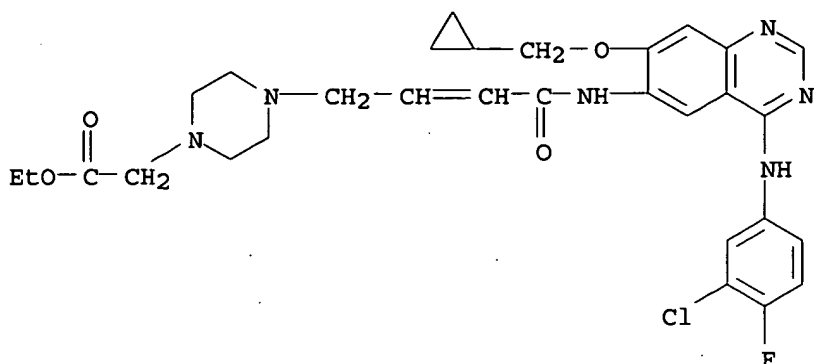
RN 290301-96-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(2-ethoxy-4-morpholinyl)- (9CI) (CA INDEX NAME)



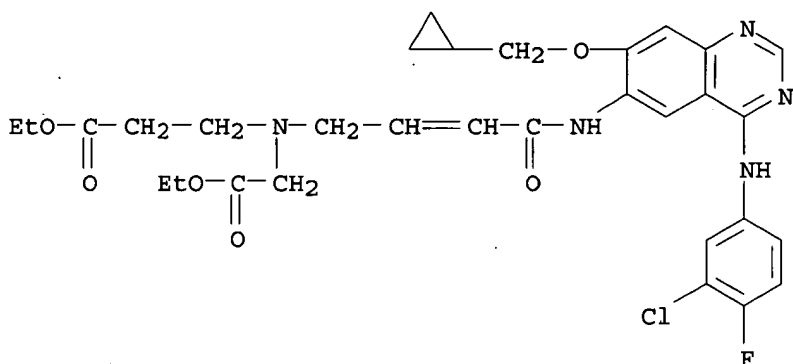
RN 290302-11-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



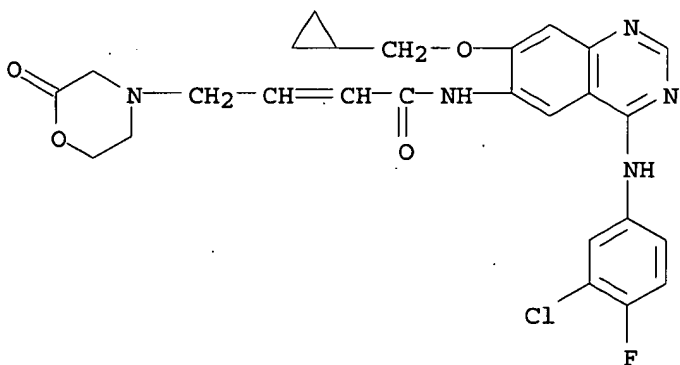
RN 290302-19-1 CAPLUS

CN .beta.-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



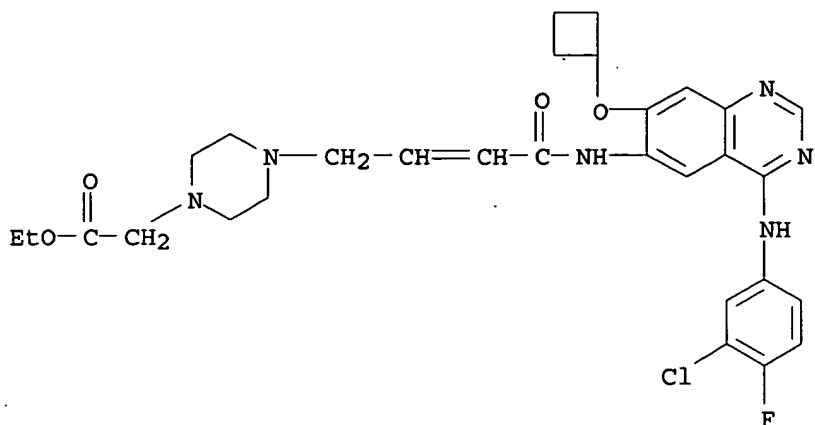
RN 290302-25-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



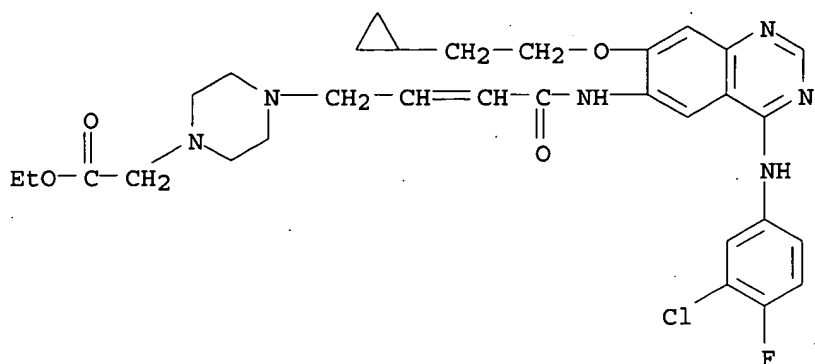
RN 290302-33-9 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-39-5 CAPLUS

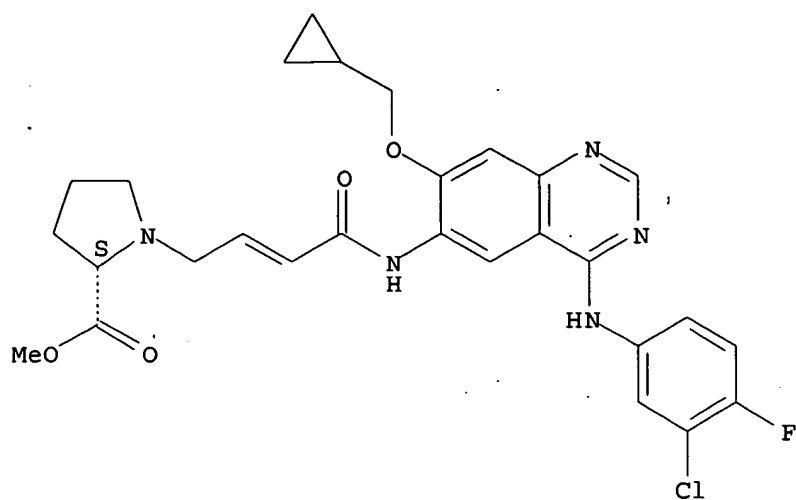
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(2-cyclopropylethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



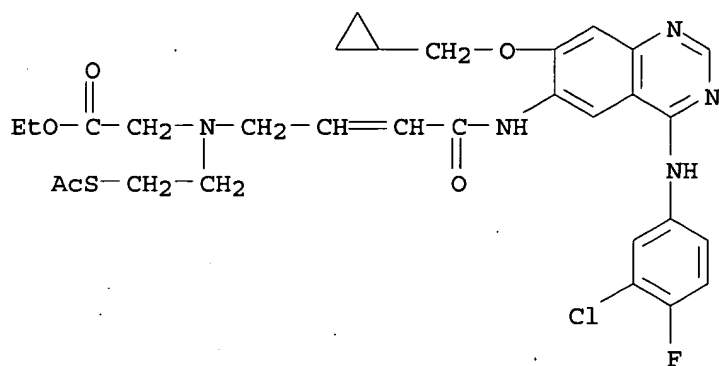
RN 290302-47-5 CAPLUS

CN L-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

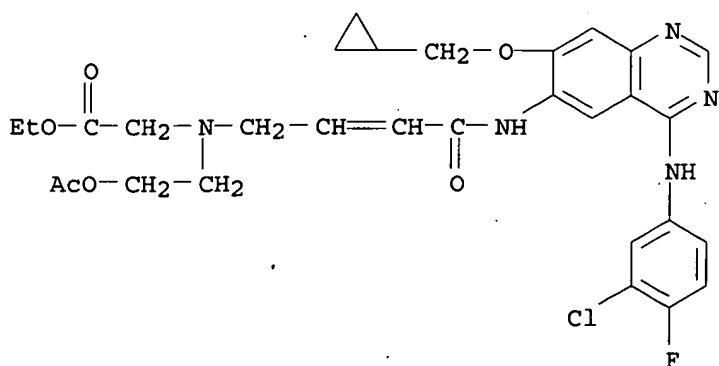
Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-98-6 CAPLUS
 CN Glycine, N-[2-(acetylthio)ethyl]-N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290303-04-7 CAPLUS
 CN Glycine, N-[2-(acetyloxy)ethyl]-N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



10/ 023,099

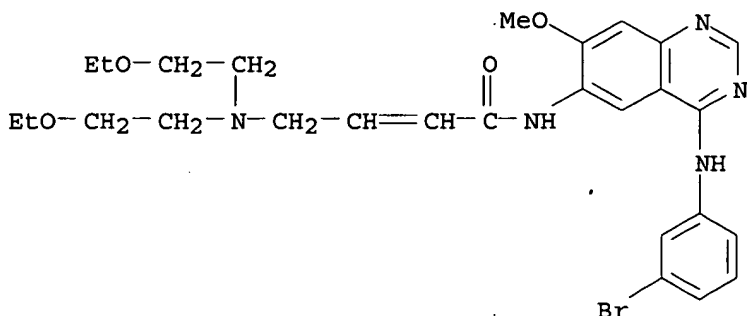
IT 290304-09-5 290304-10-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

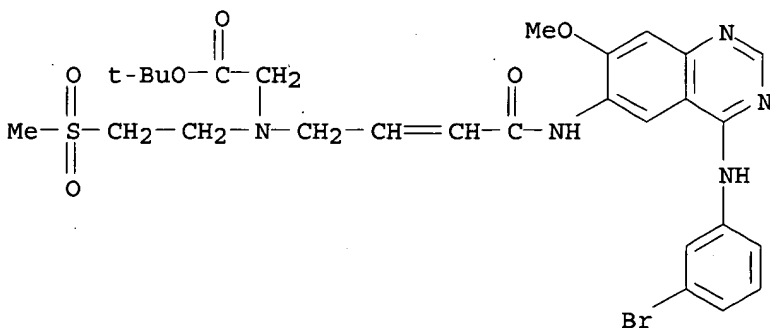
RN 290304-09-5 CAPLUS.

CN 2-Butenamide, 4-[bis(2-ethoxyethyl)amino]-N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 290304-10-8 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-(methylsulfonyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 290303-47-8P 290303-83-2P 290303-84-3P

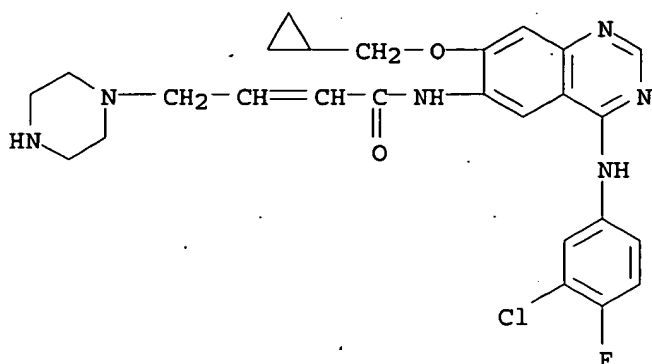
290304-01-7P 290304-02-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

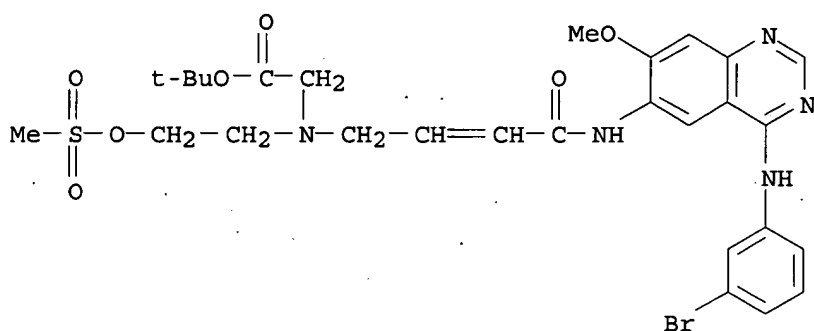
RN 290303-47-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)



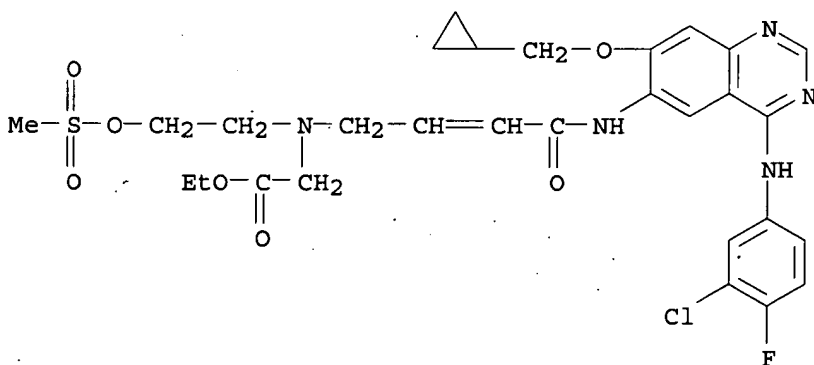
RN 290303-83-2 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-[(methylsulfonyl)oxy]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



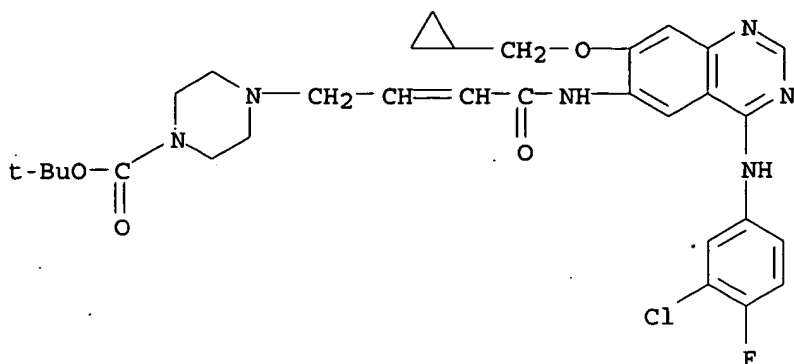
RN 290303-84-3 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-[(methylsulfonyl)oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

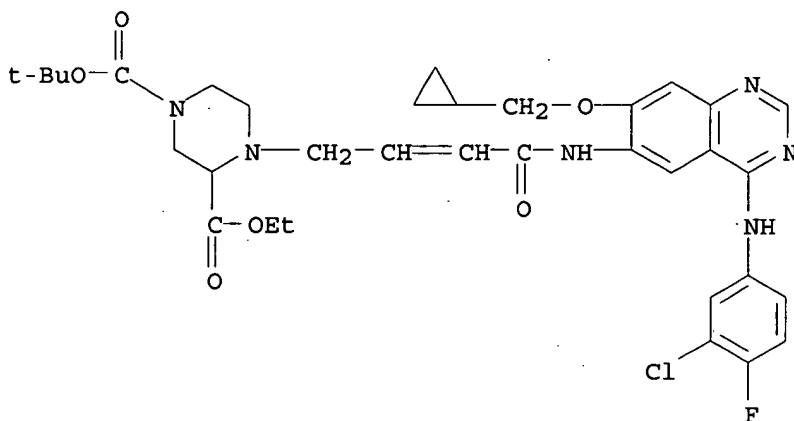


RN 290304-01-7 CAPLUS

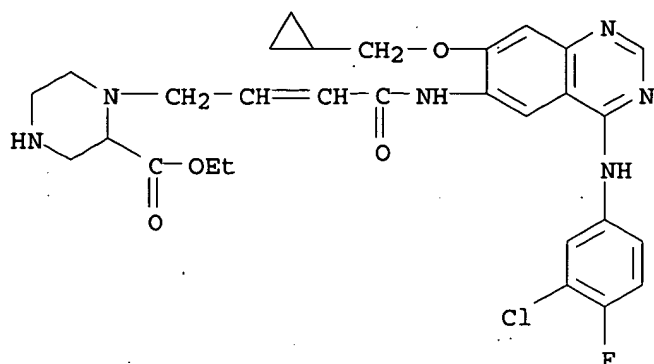
CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 290304-02-8 CAPLUS
 CN 1,3-Piperazinedicarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1-(1,1-dimethylethyl) 3-ethyl ester (9CI) (CA INDEX NAME)



IT 290303-13-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)
 (prepn. of aminoquinazoline and aminoquinoline derivs. having an
 inhibitory effect on signal transduction mediated by tyrosine kinases
 useful for treating tumoral diseases, lung and respiratory tract
 diseases)
 RN 290303-13-8 CAPLUS
 CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT 289700-69-2P 290301-73-4P 290301-74-5P
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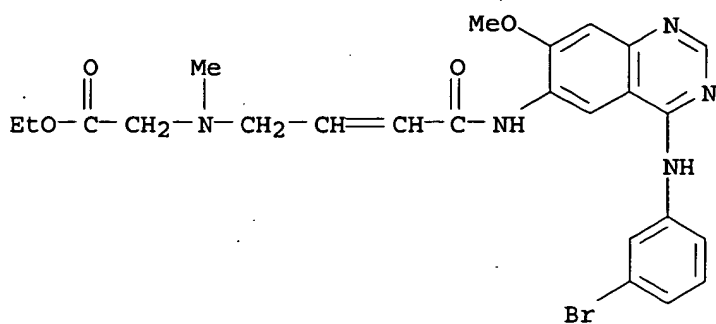
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 289700-69-2 CAPLUS

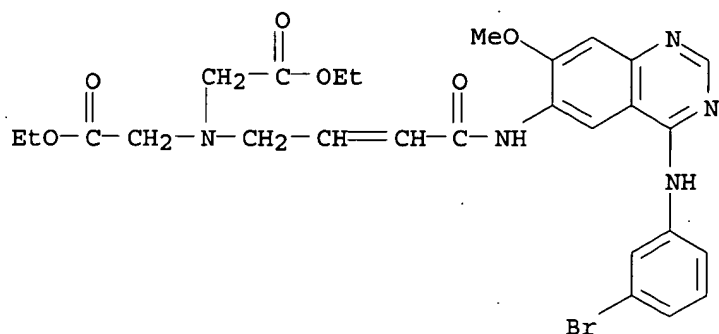
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

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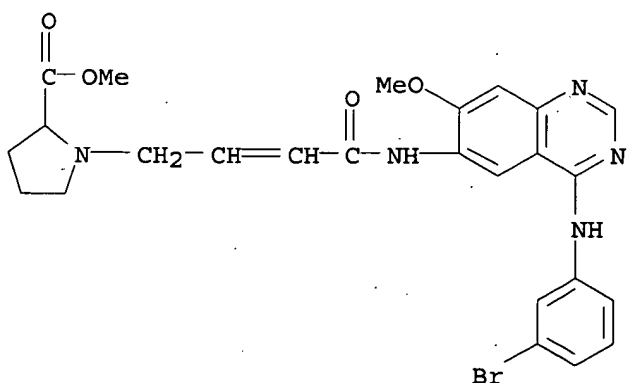
RN 290301-73-4 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



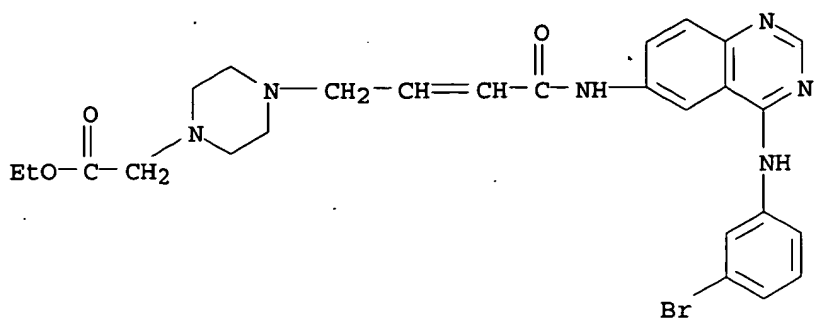
RN 290301-74-5 CAPLUS

CN Proline, 1-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)



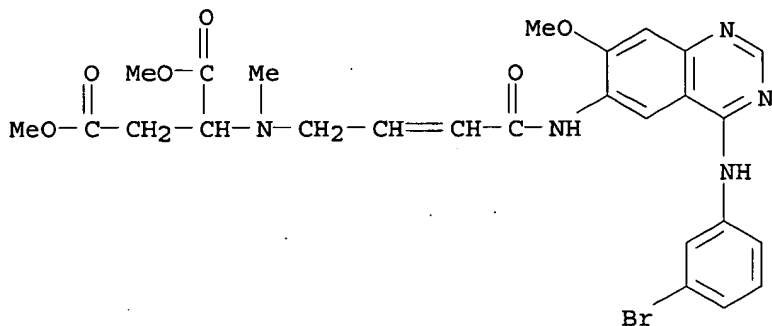
RN 290301-76-7 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



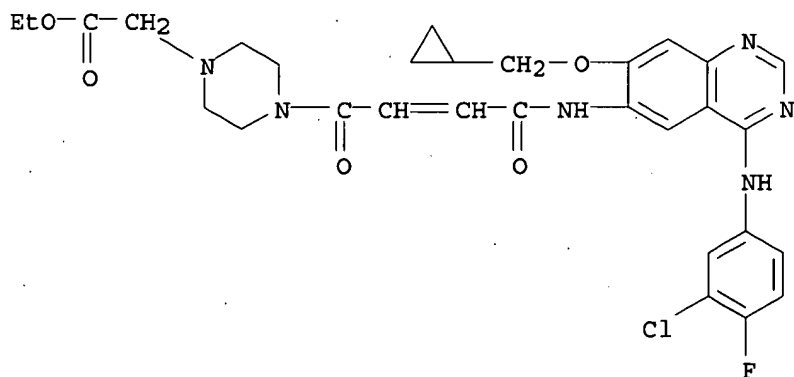
RN 290301-77-8 CAPLUS

CN Aspartic acid, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, dimethyl ester (9CI) (CA INDEX NAME)



RN 290301-81-4 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

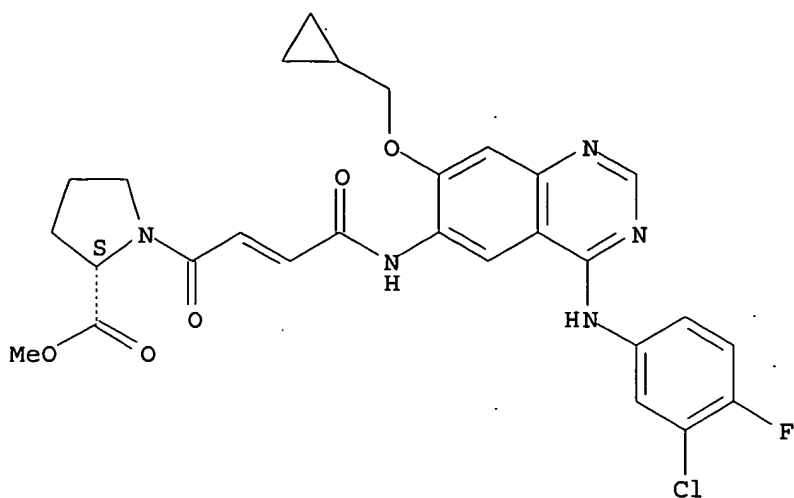


RN 290301-82-5 CAPLUS

CN L-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

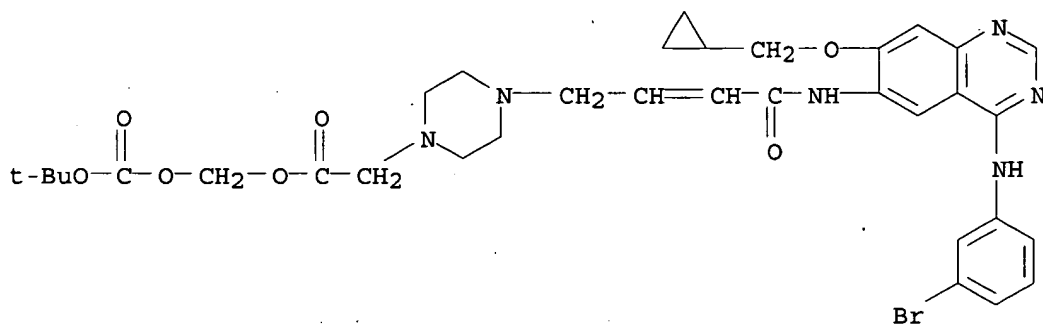
Absolute stereochemistry.

Double bond geometry unknown.



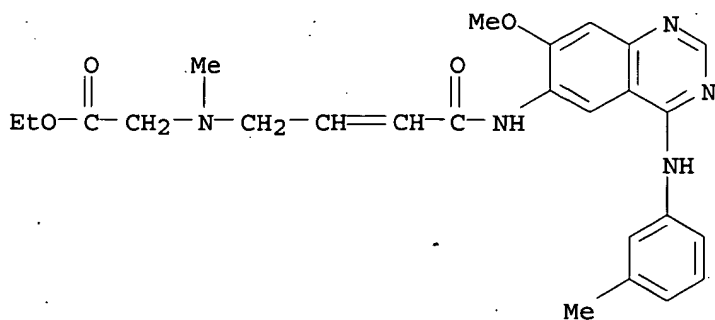
RN 290301-85-8 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, [(1,1-dimethylethoxy)carbonyl]oxy]methyl ester (9CI) (CA INDEX NAME)



RN 290301-86-9 CAPLUS

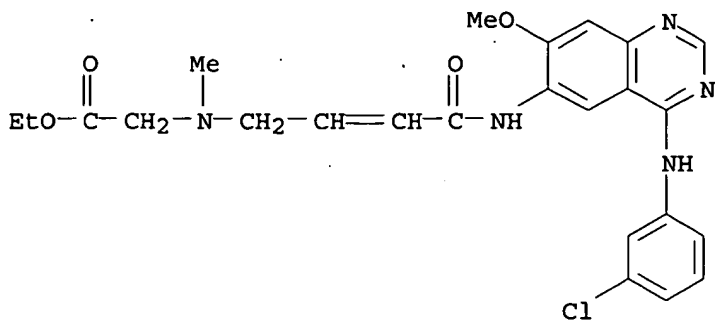
CN Glycine, N-[4-[[7-methoxy-4-[(3-methylphenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 290301-87-0 CAPLUS

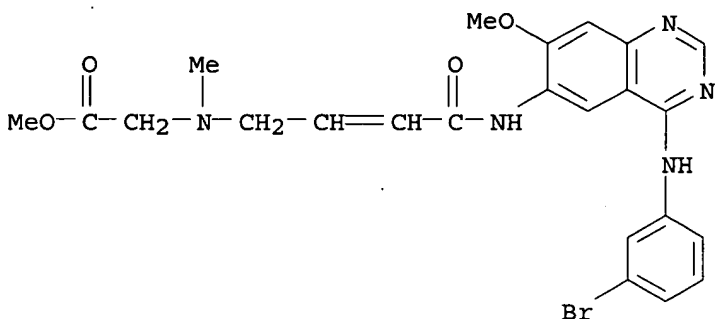
CN Glycine, N-[4-[[4-[(3-chlorophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

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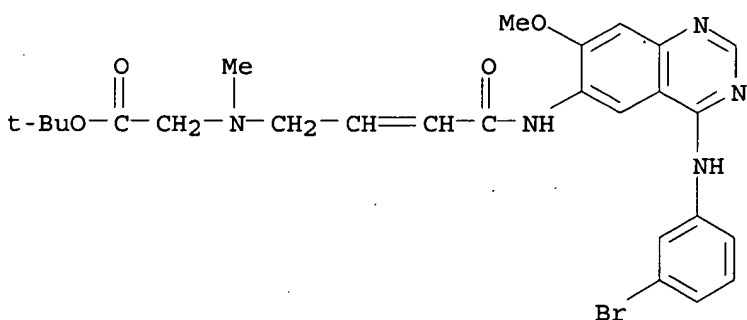
RN 290301-89-2 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)



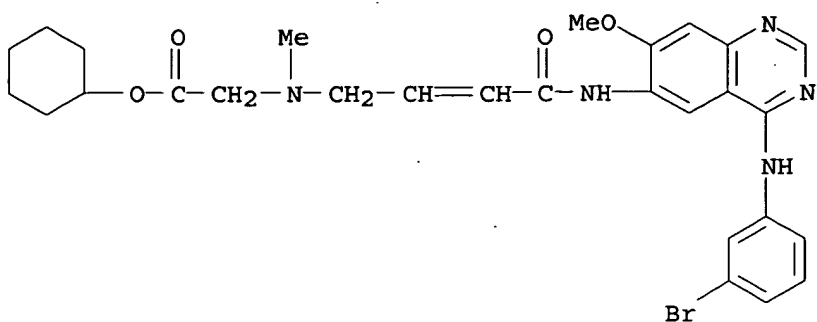
RN 290301-90-5 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

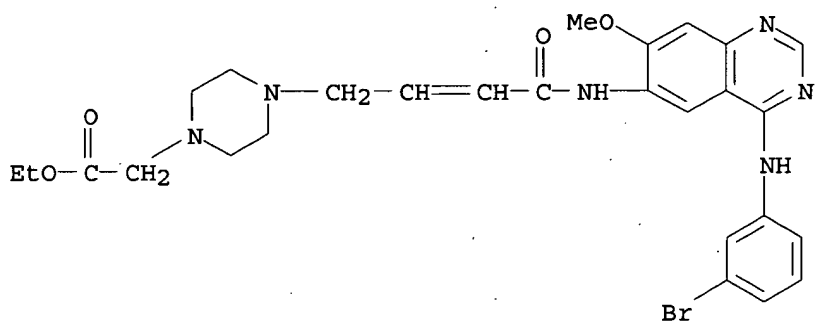


RN 290301-91-6 CAPLUS

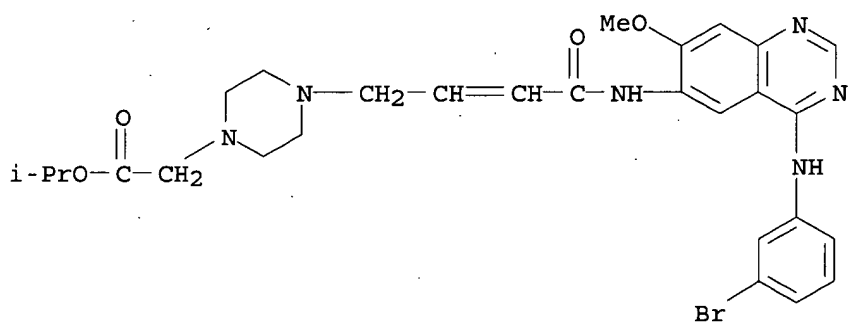
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, cyclohexyl ester (9CI) (CA INDEX NAME)



RN 290301-92-7 CAPLUS
 CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

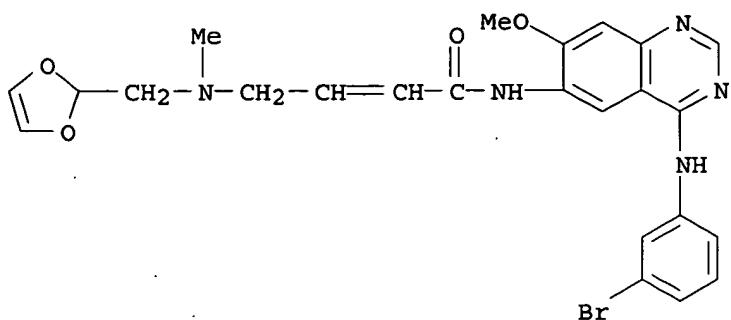


RN 290301-93-8 CAPLUS
 CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)



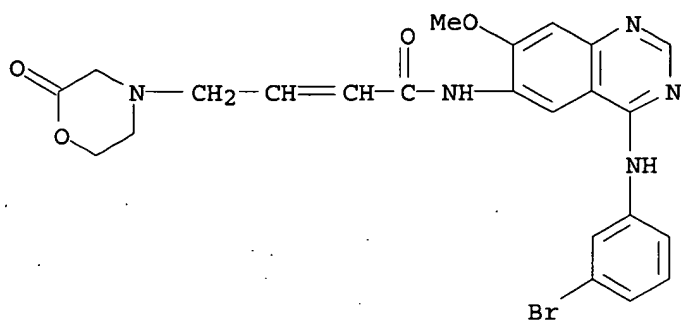
RN 290301-95-0 CAPLUS
 CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(1,3-dioxol-2-ylmethyl)methylamino]- (9CI) (CA INDEX NAME)

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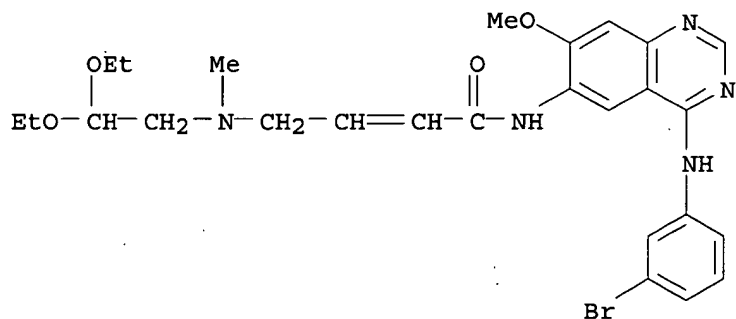
RN 290301-98-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



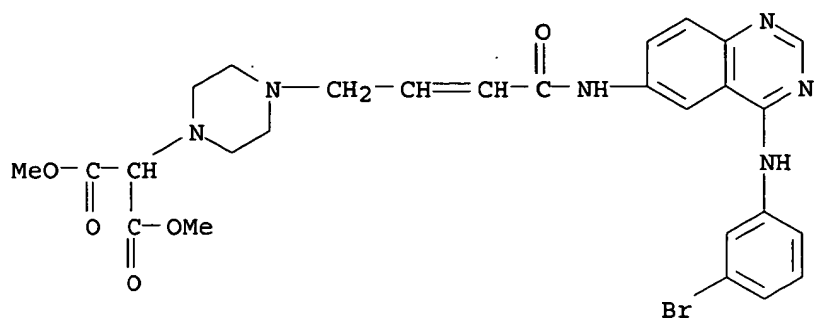
RN 290302-01-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(2,2-diethoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



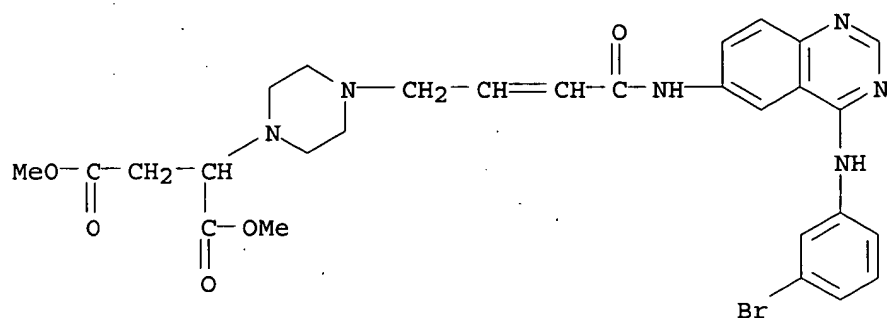
RN 290302-03-3 CAPLUS

CN Propanedioic acid, [4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]-, dimethyl ester (9CI) (CA INDEX NAME)



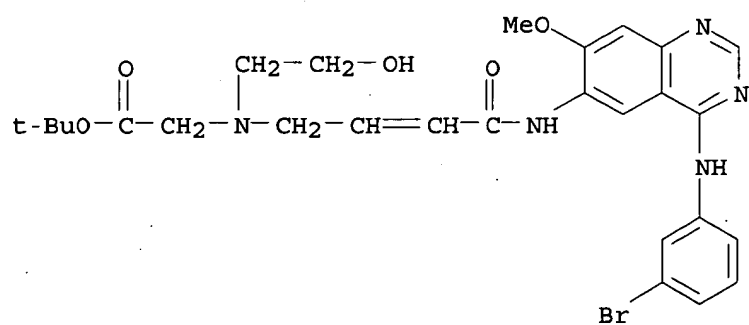
RN 290302-05-5 CAPLUS

CN Butanedioic acid, [4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]-, dimethyl ester (9CI) (CA INDEX NAME)



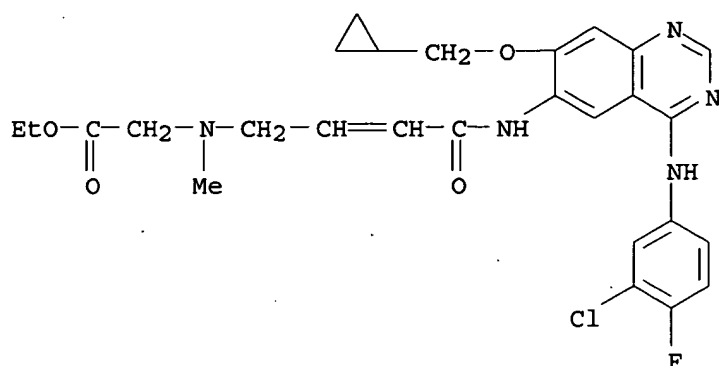
RN 290302-07-7 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



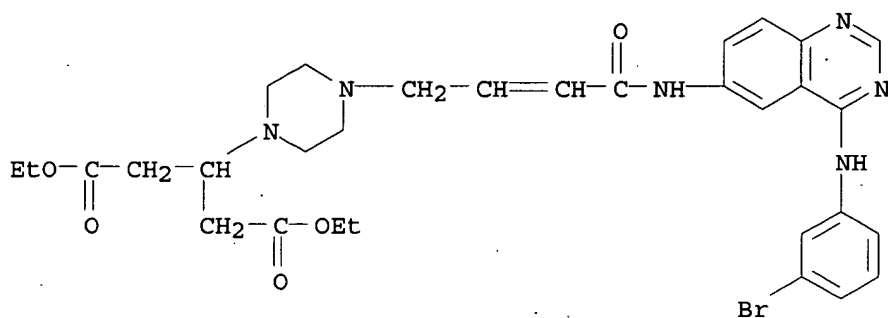
RN 290302-09-9 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



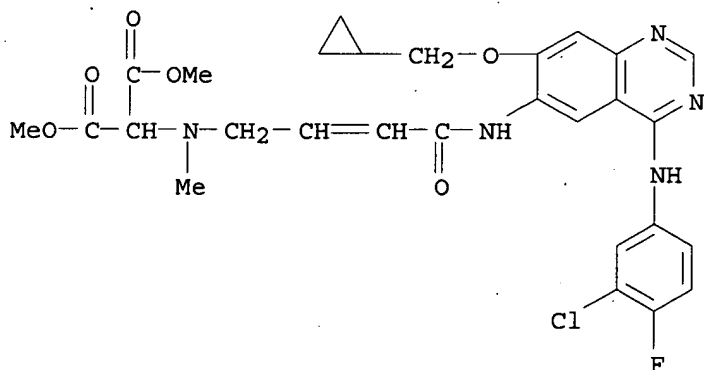
RN 290302-13-5 CAPLUS

CN Pentanedioic acid, 3-[4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]-, diethyl ester (9CI)
(CA INDEX NAME)



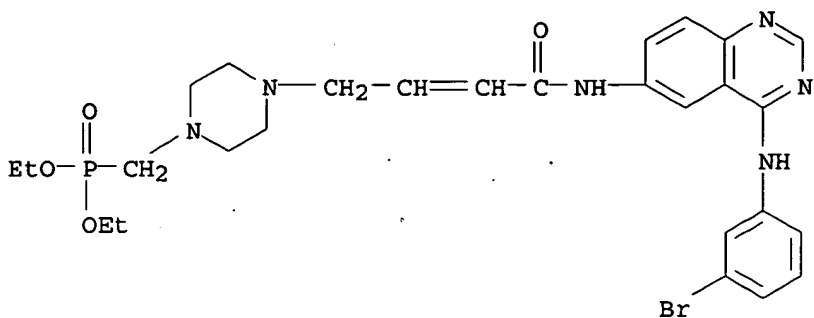
RN 290302-15-7 CAPLUS

CN Propanedioic acid, [[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]-, dimethyl ester (9CI) (CA INDEX NAME)



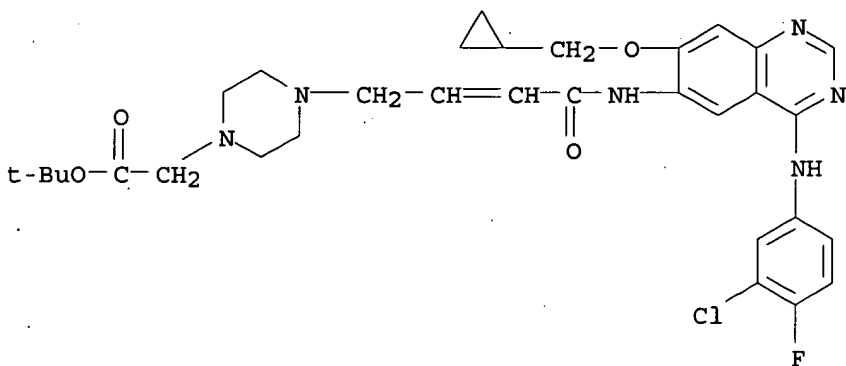
RN 290302-17-9 CAPLUS

CN Phosphonic acid, [[4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



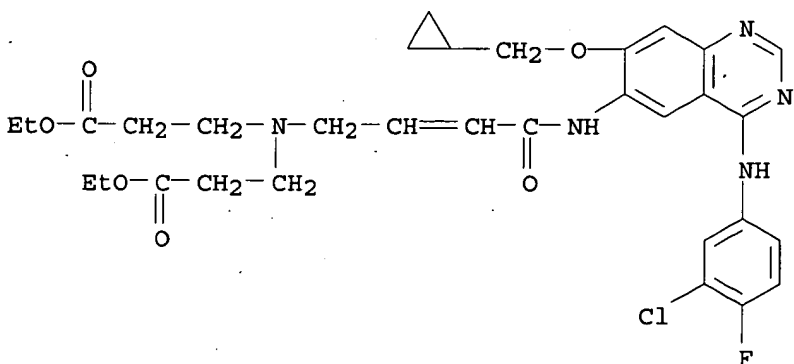
RN 290302-21-5 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



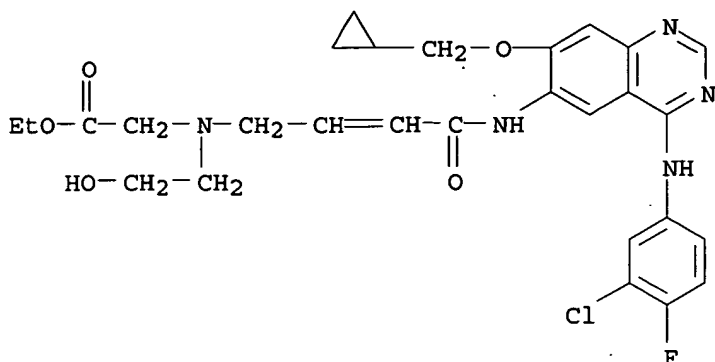
RN 290302-23-7 CAPLUS

CN .beta.-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(3-ethoxy-3-oxopropyl)-, ethyl ester (9CI) (CA INDEX NAME)



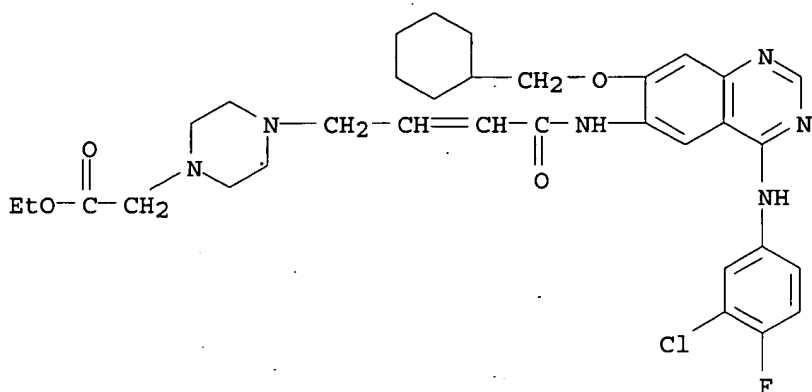
RN 290302-27-1 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)



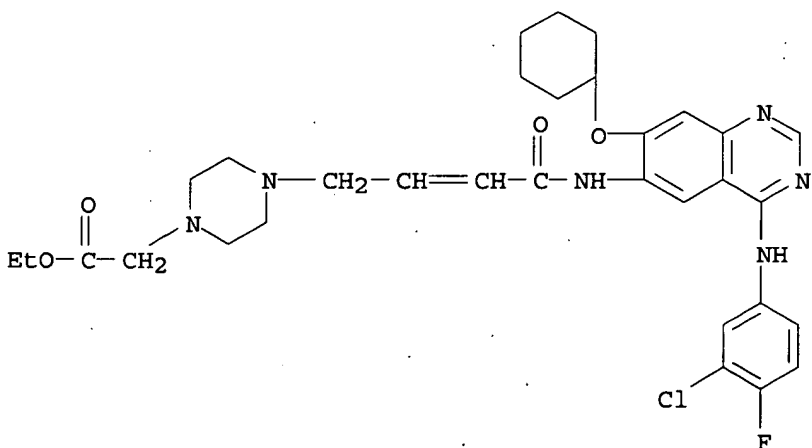
RN 290302-29-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclohexylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-31-7 CAPLUS

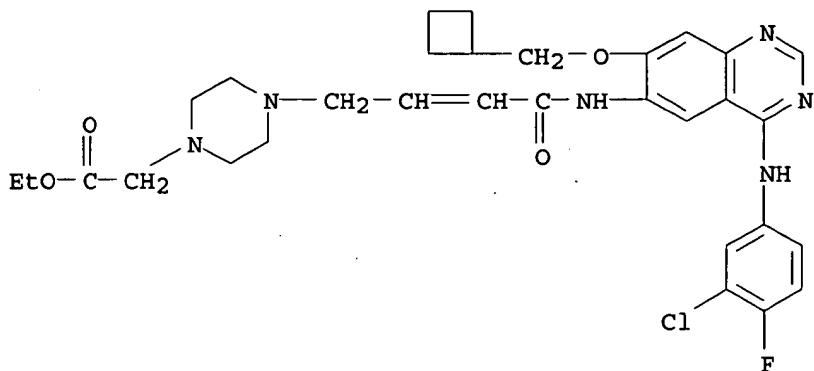
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclohexyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-35-1 CAPLUS

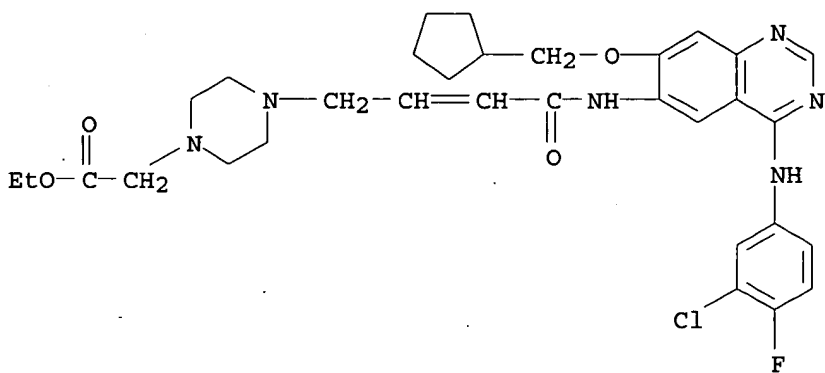
10/ 023,099

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester
(9CI) (CA INDEX NAME)



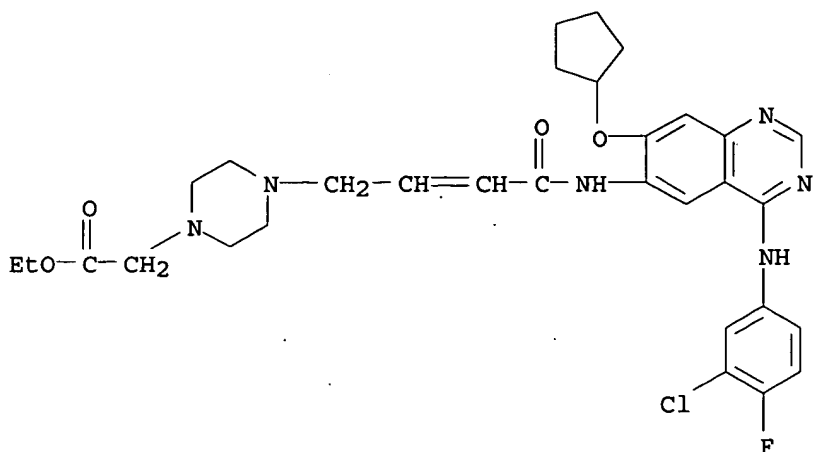
RN 290302-37-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester
(9CI) (CA INDEX NAME)



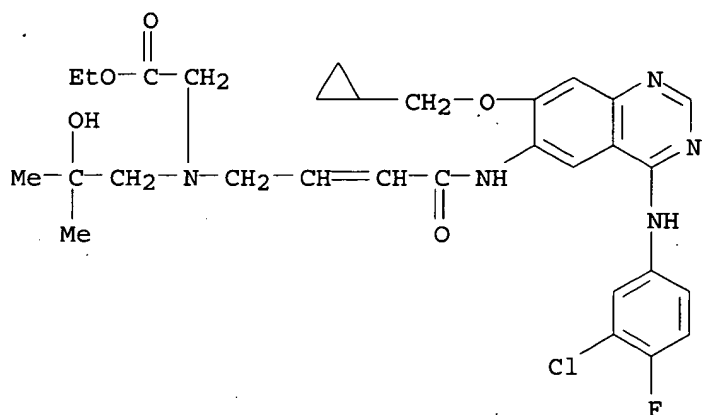
RN 290302-41-9 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester
(9CI) (CA INDEX NAME)



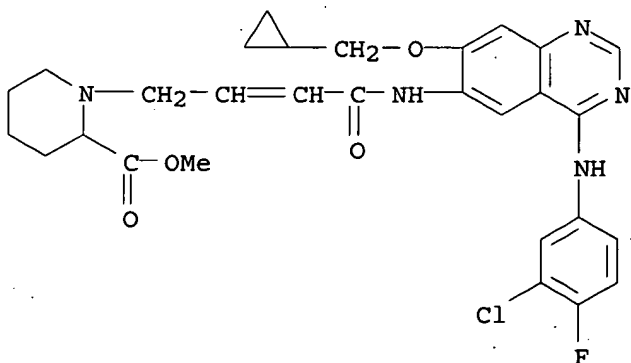
RN 290302-43-1 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-45-3 CAPLUS

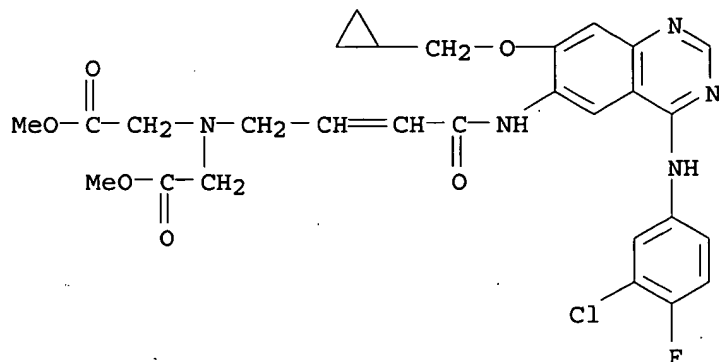
CN 2-Piperidinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)



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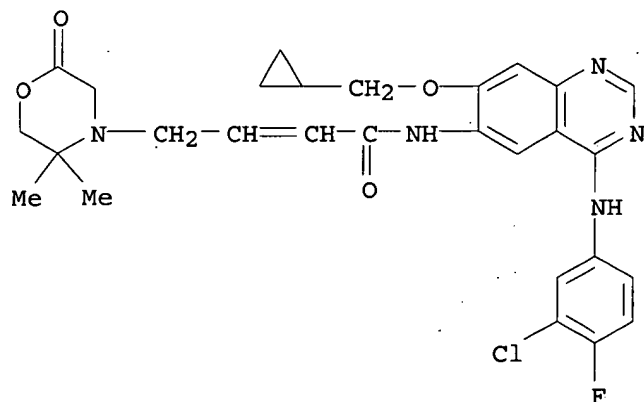
RN 290302-49-7 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-methoxy-2-oxoethyl)-, methyl ester (9CI) (CA INDEX NAME)



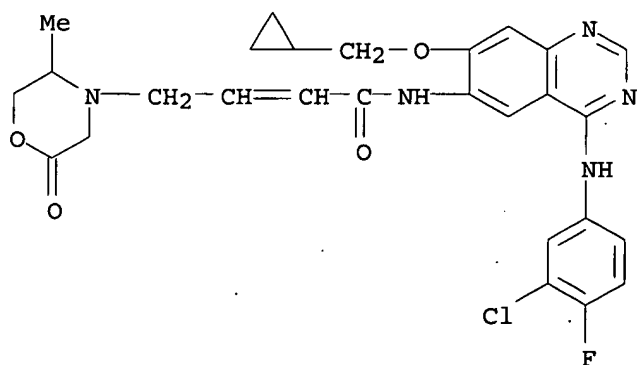
RN 290302-51-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 290302-53-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5-methyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

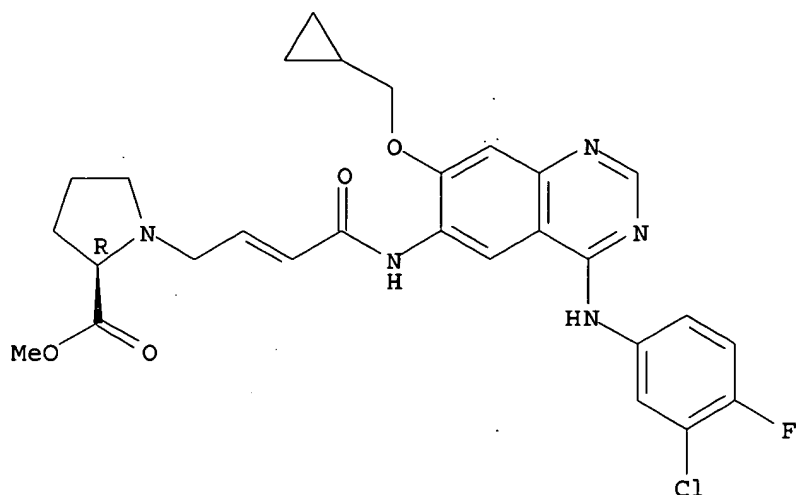


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RN 290302-55-5 CAPLUS

CN D-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

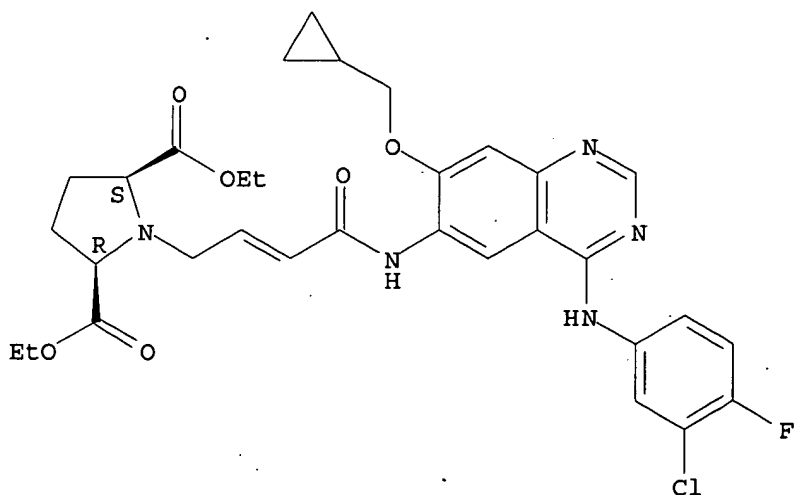
Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-57-7 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, diethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

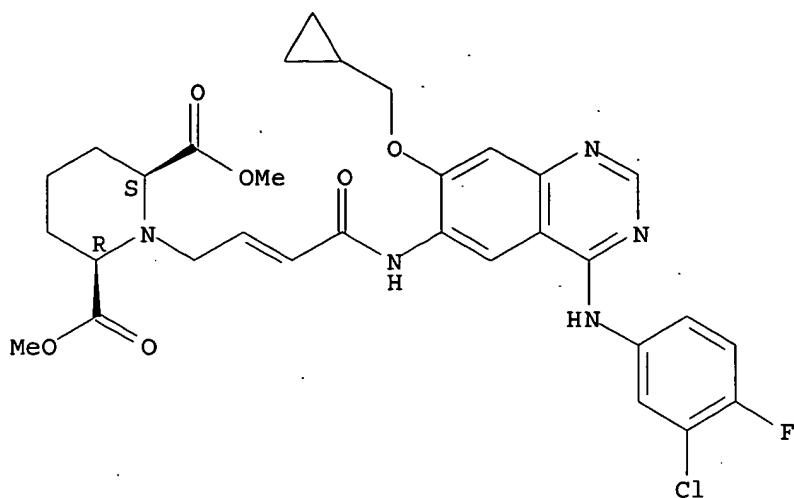
Relative stereochemistry.
Double bond geometry unknown.



RN 290302-59-9 CAPLUS

CN 2,6-Piperidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.

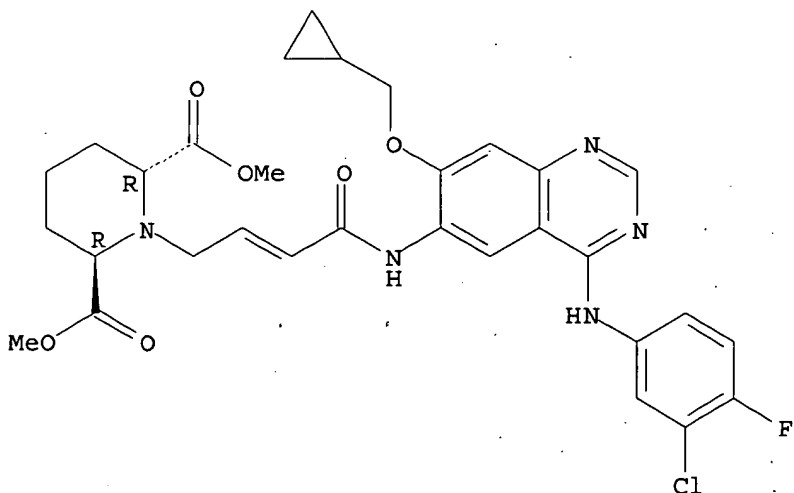


RN 290302-61-3 CAPLUS

CN 2,6-Piperidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry unknown.

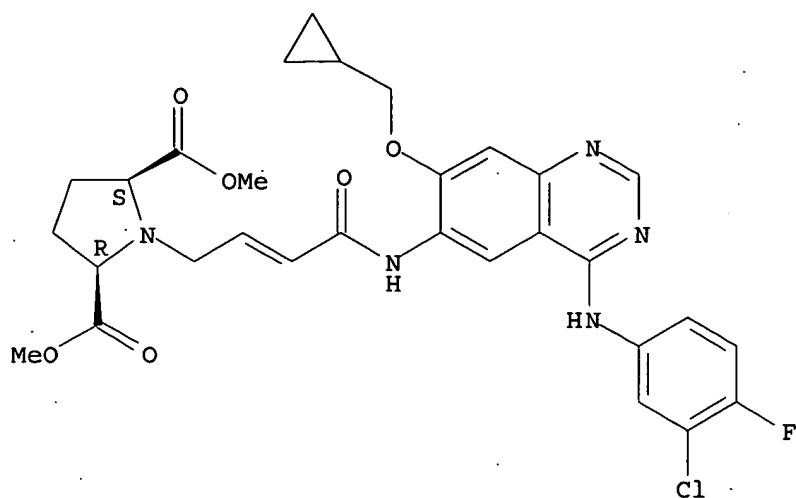


RN 290302-63-5 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry unknown.

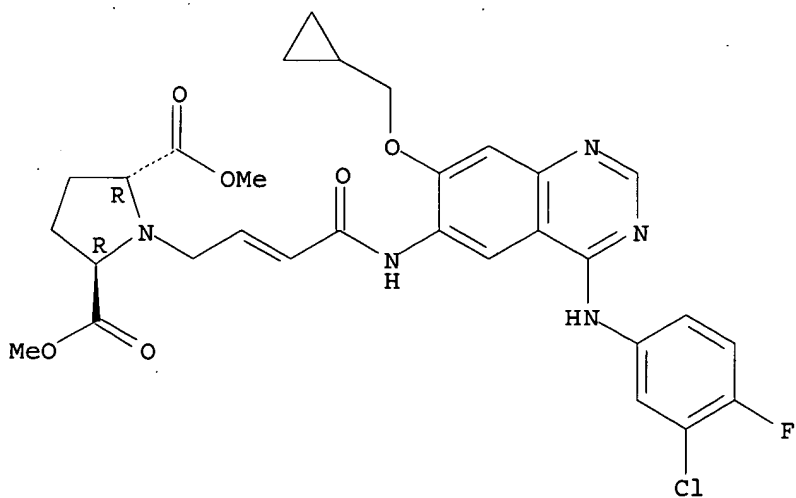


RN 290302-65-7 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

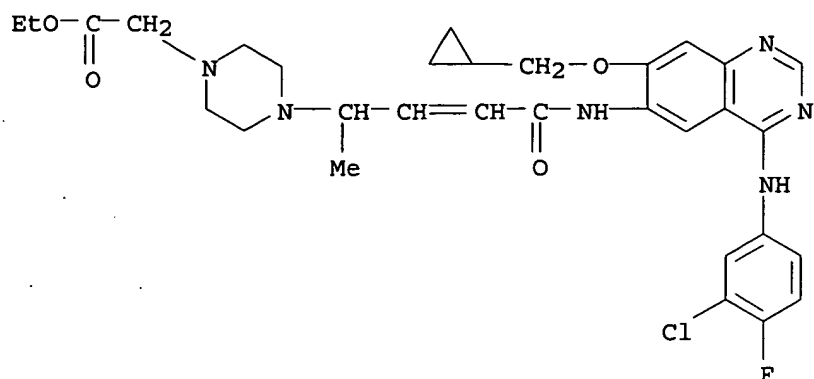
Double bond geometry unknown.



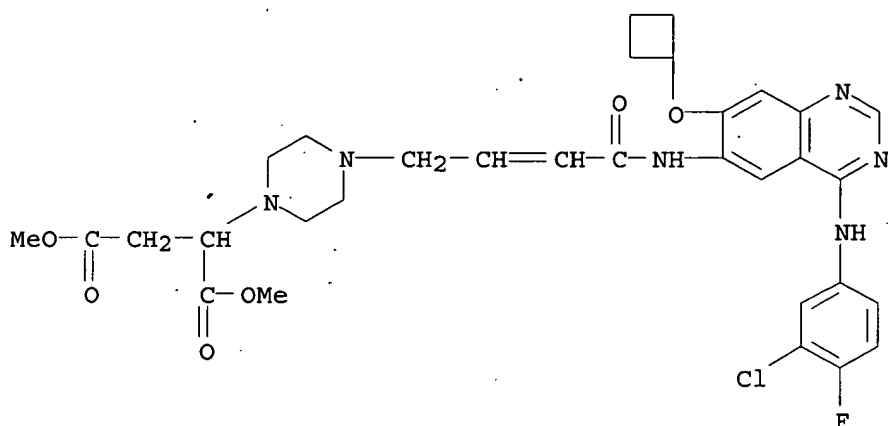
RN 290302-67-9 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1-methyl-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

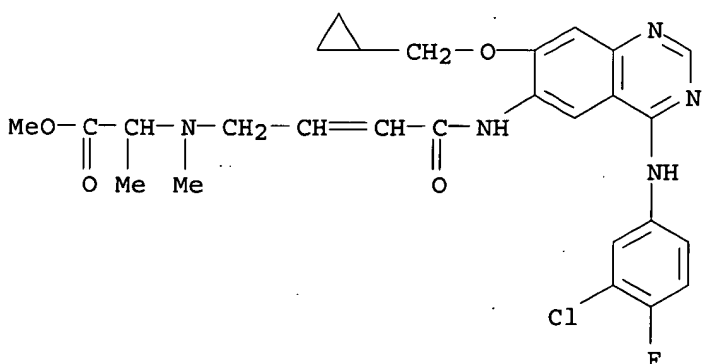
10/ 023,099



RN 290302-69-1 CAPLUS
 CN Butanedioic acid, [4-[4-[[4-[(3-chloro-4-fluorophényl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 290302-71-5 CAPLUS
 CN Alanine, N-[4-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)

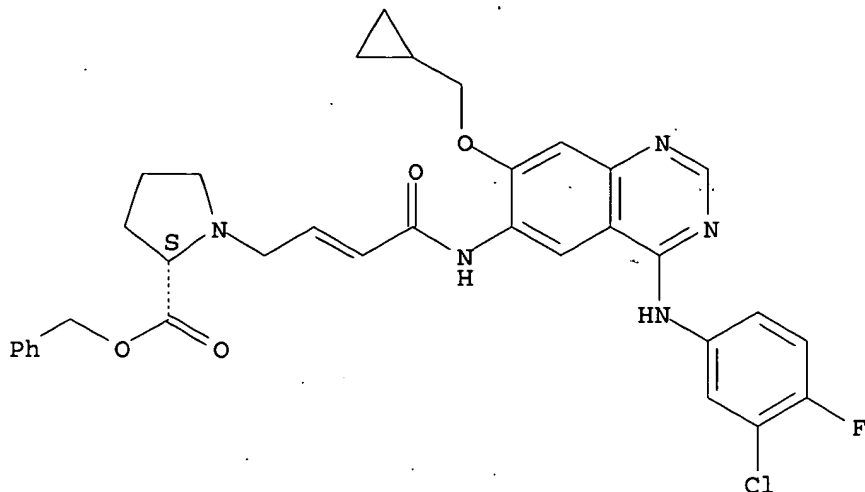


RN 290302-73-7 CAPLUS
 CN L-Proline, 1-[4-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenylmethyl

10/ 023,099

ester (9CI) (CA INDEX NAME)

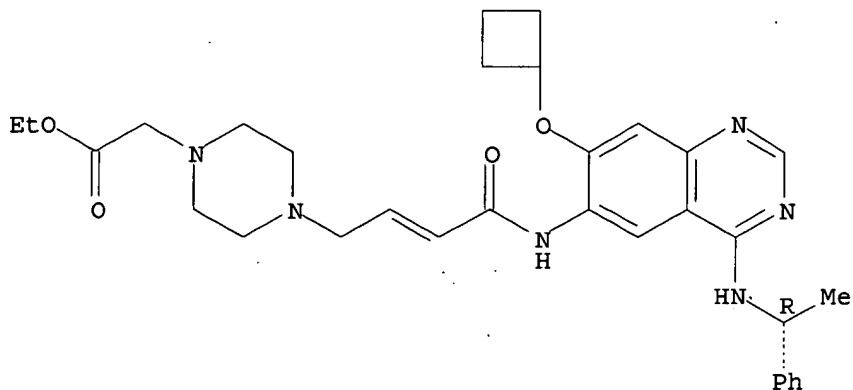
Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-75-9 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[7-(cyclobutyloxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

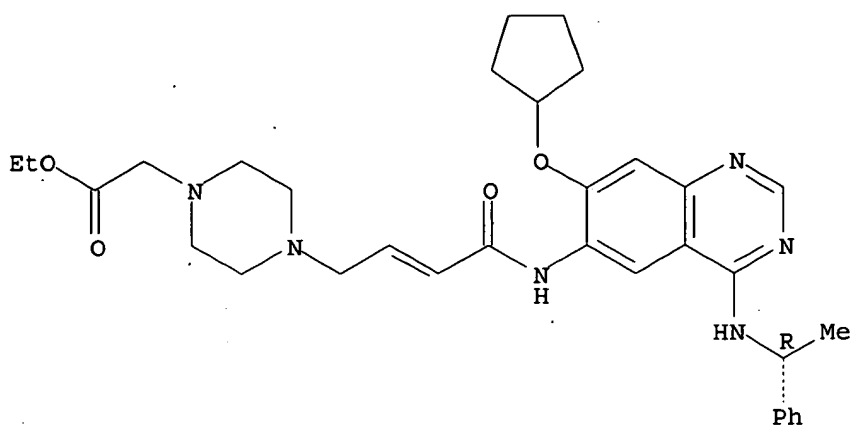
Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-77-1 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[7-(cyclopentyloxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

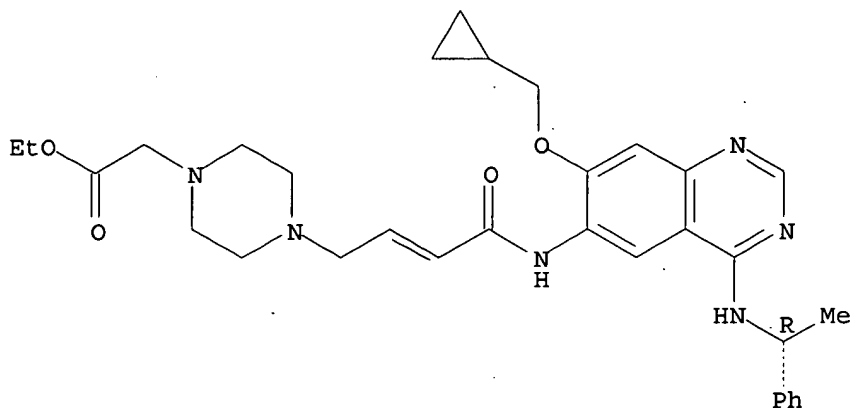
Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-79-3 CAPLUS

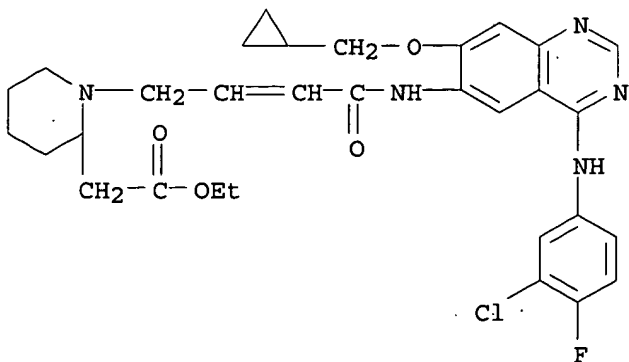
CN 1-Piperazineacetic acid, 4-[4-[[7-(cyclopropylmethoxy)-4-[[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



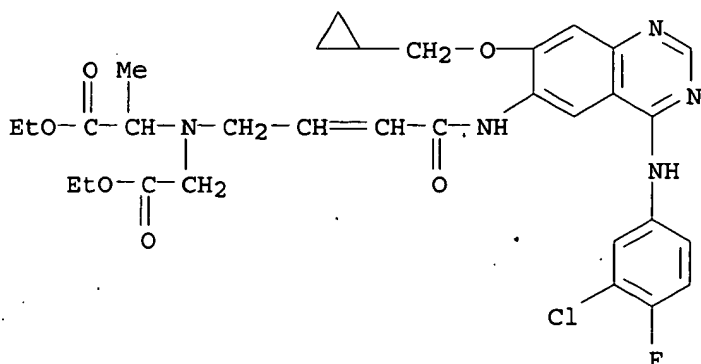
RN 290302-81-7 CAPLUS

CN 2-Piperidineacetic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester
(9CI) (CA INDEX NAME)



RN 290302-83-9 CAPLUS

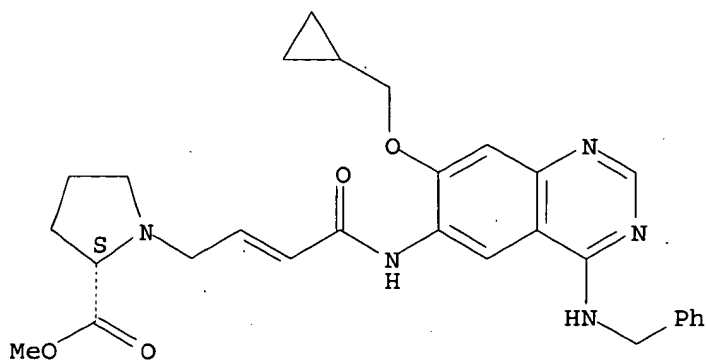
CN Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-85-1 CAPLUS

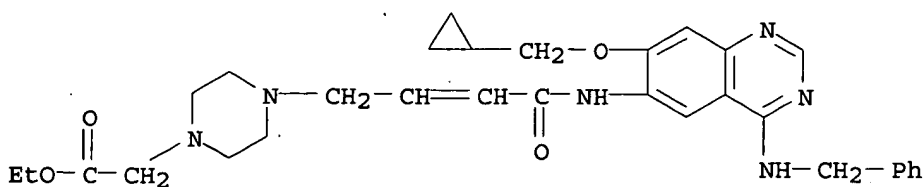
CN L-Proline, 1-[4-[[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-87-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

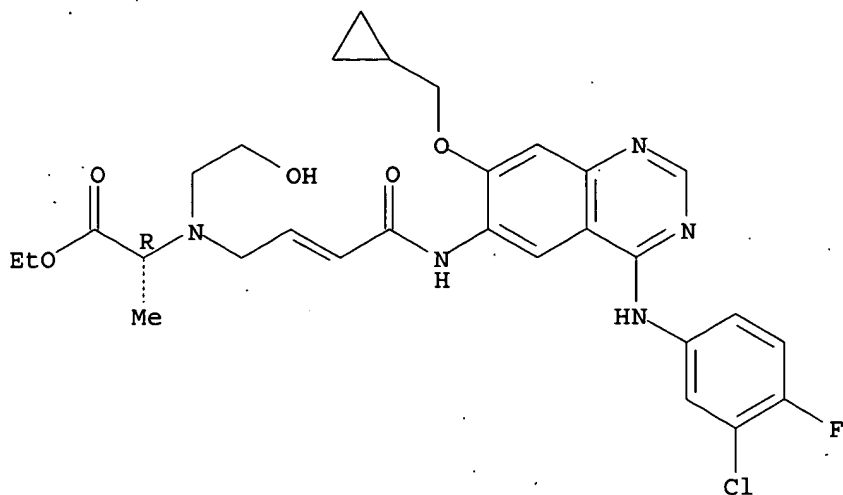


RN 290302-89-5 CAPLUS

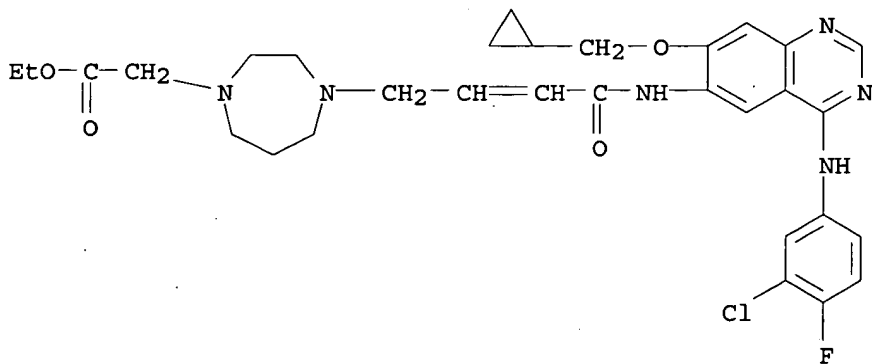
CN D-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

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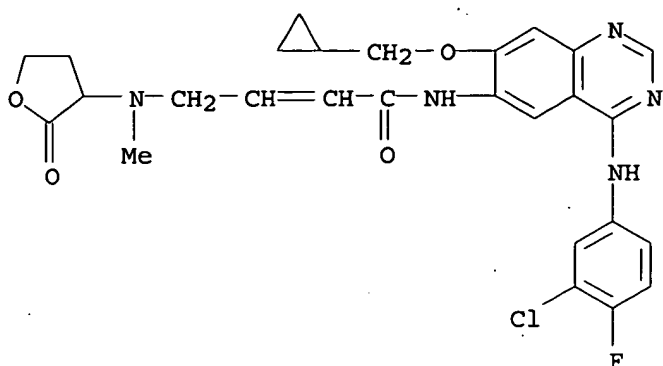
Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-91-9 CAPLUS
CN 1H-1,4-Diazepine-1-acetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]hexahydro-, ethyl ester (9CI) (CA INDEX NAME)

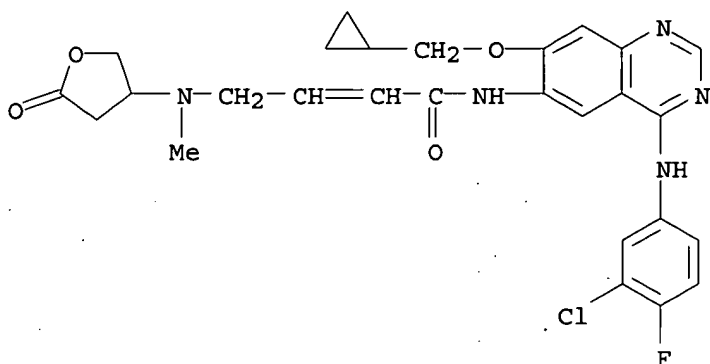


RN 290302-93-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]- (9CI) (CA INDEX NAME)



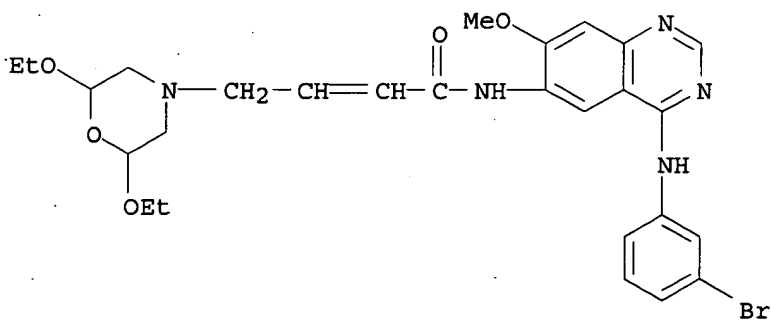
RN 290302-94-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-5-oxo-3-furanyl)amino]-(9CI) (CA INDEX NAME)



RN 290302-96-4 CAPLUS

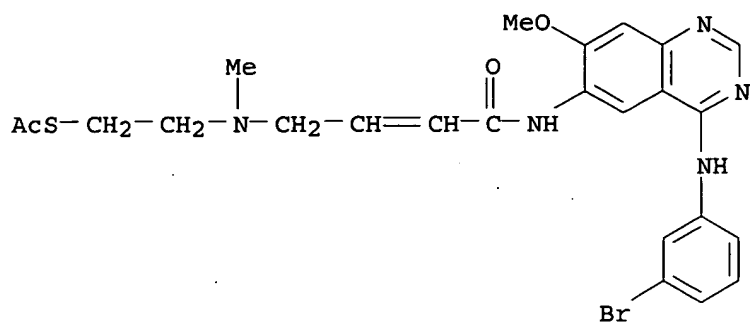
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(2,6-diethoxy-4-morpholinyl)-(9CI) (CA INDEX NAME)



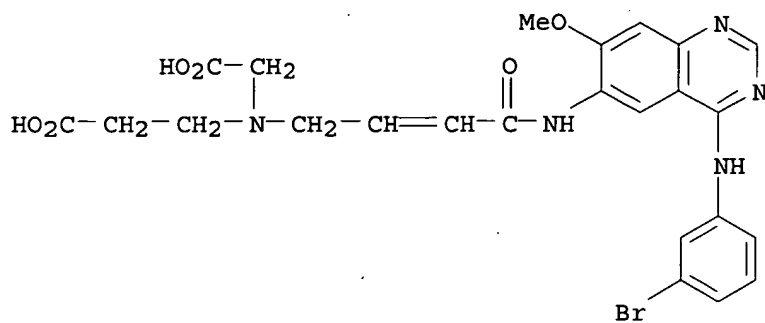
RN 290302-97-5 CAPLUS

CN Ethanethioic acid, S-[2-[[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]ethyl] ester (9CI) (CA INDEX NAME)

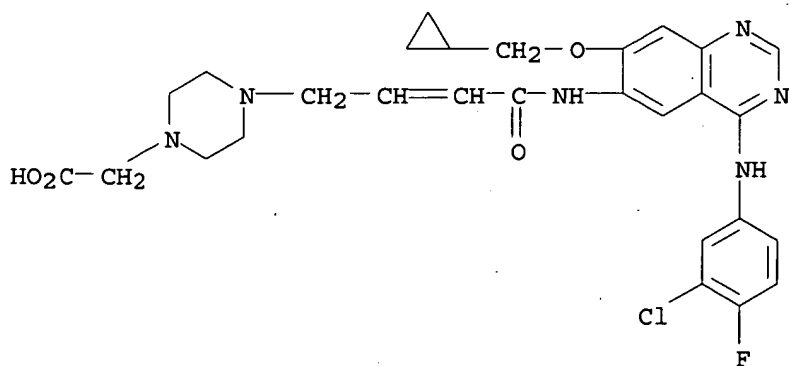
10/ 023,099



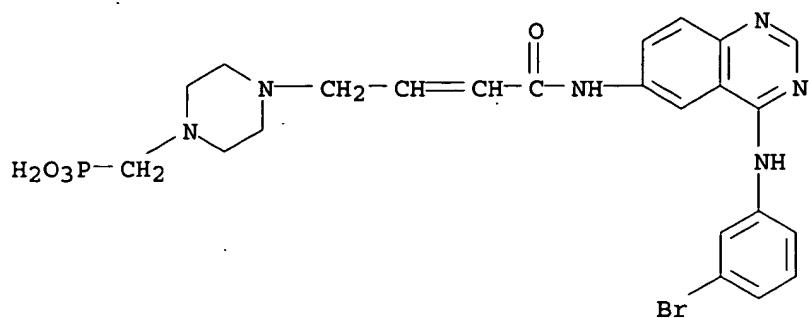
RN 290302-99-7 CAPLUS
 CN .beta.-Alanine, N-[[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(carboxymethyl)- (9CI) (CA INDEX NAME)



RN 290303-00-3 CAPLUS
 CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)

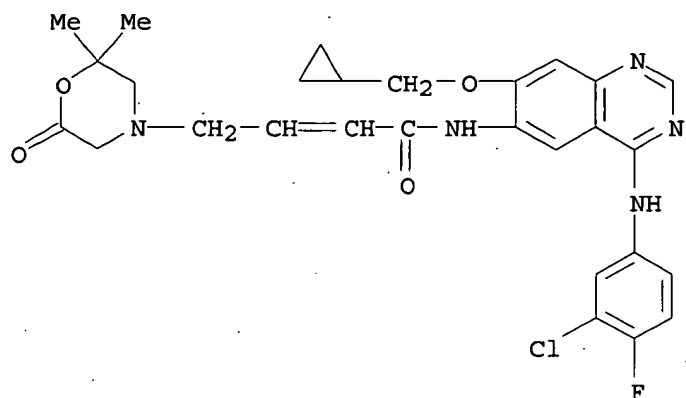


RN 290303-01-4 CAPLUS
 CN Phosphonic acid, [[4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



RN 290303-02-5 CAPLUS

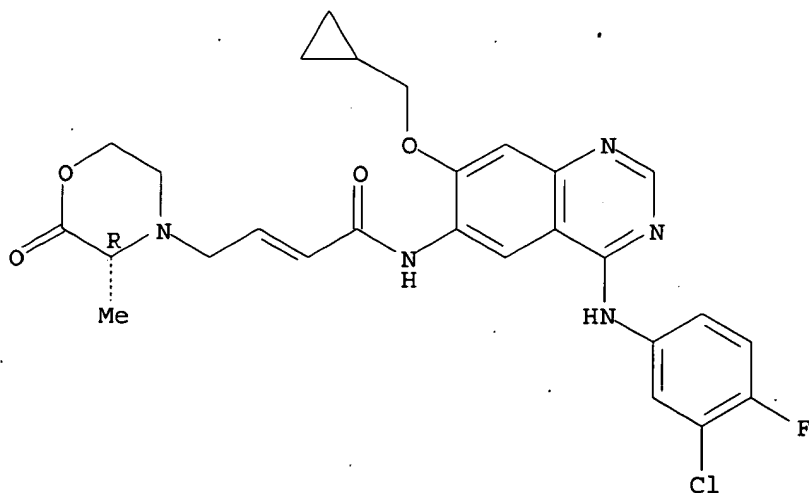
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 290303-03-6 CAPLUS

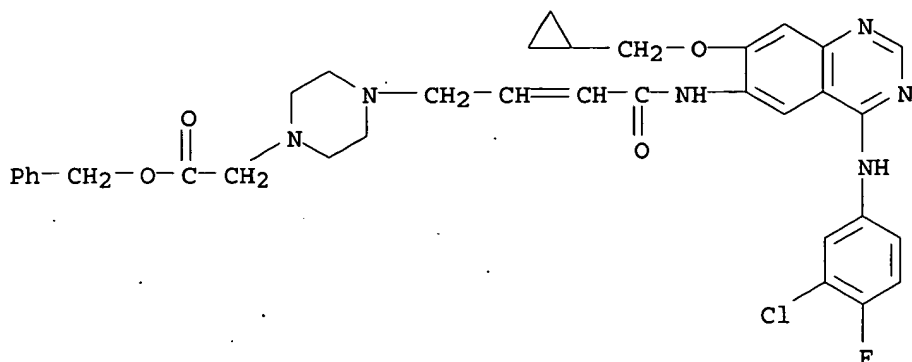
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3R)-3-methyl-2-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



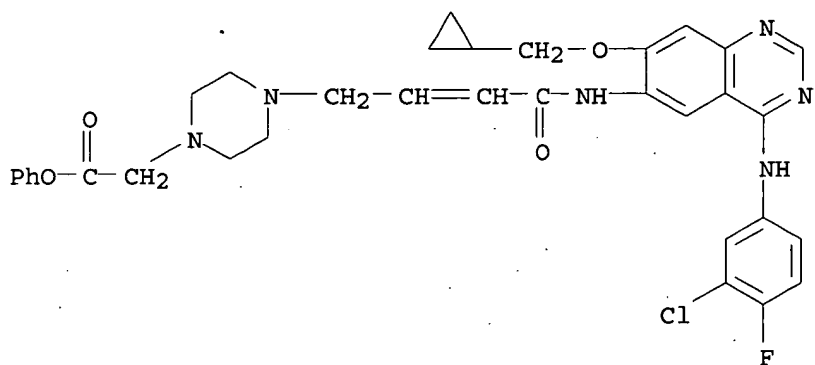
RN 290303-05-8 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



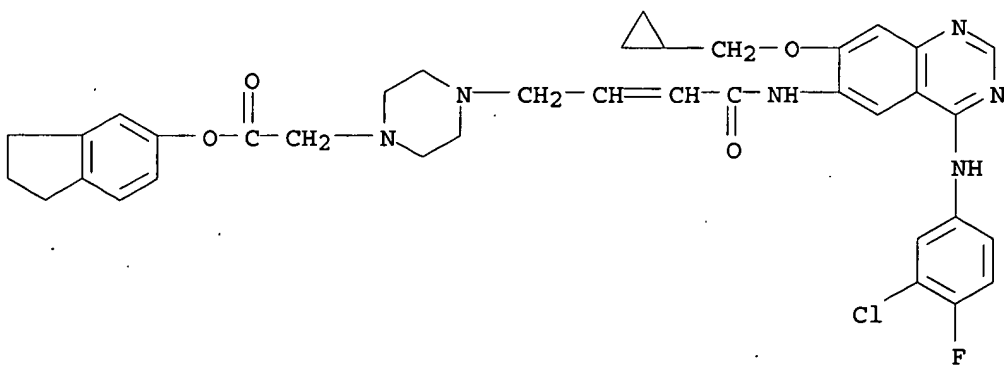
RN 290303-06-9 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenyl ester (9CI) (CA INDEX NAME)



RN 290303-07-0 CAPLUS

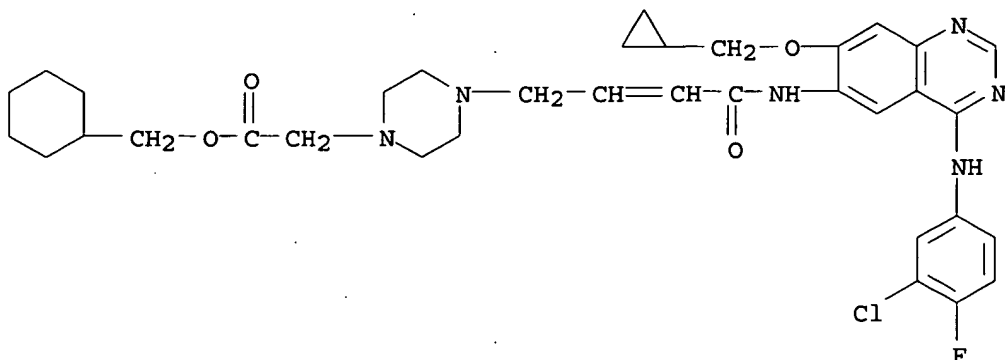
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 2,3-dihydro-1H-inden-5-yl ester (9CI) (CA INDEX NAME)



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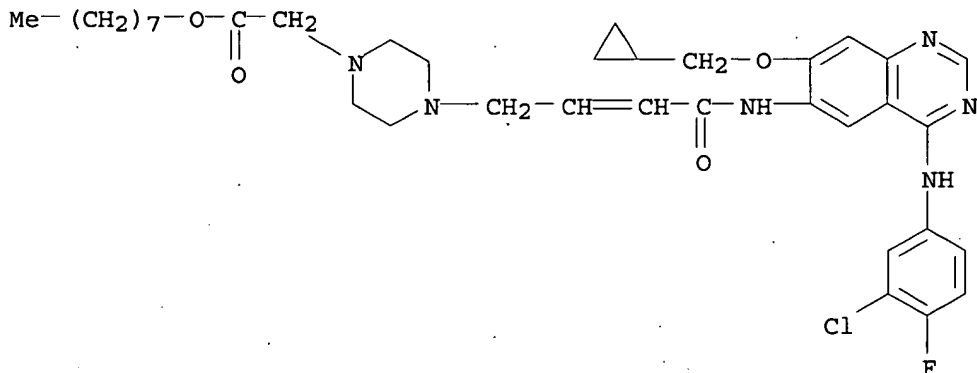
RN 290303-08-1 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, cyclohexylmethyl ester (9CI) (CA INDEX NAME)



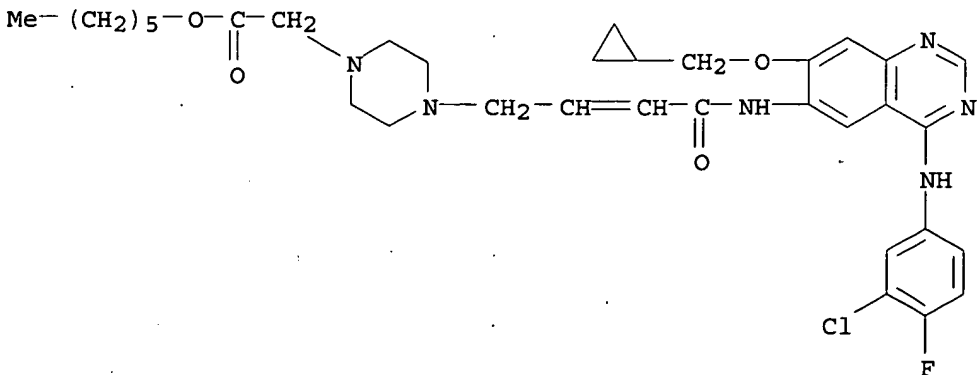
RN 290303-09-2 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, octyl ester (9CI) (CA INDEX NAME)



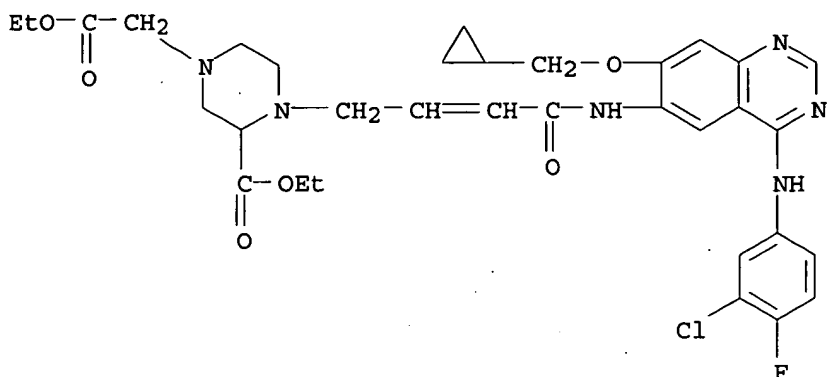
RN 290303-10-5 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, hexyl ester (9CI) (CA INDEX NAME)



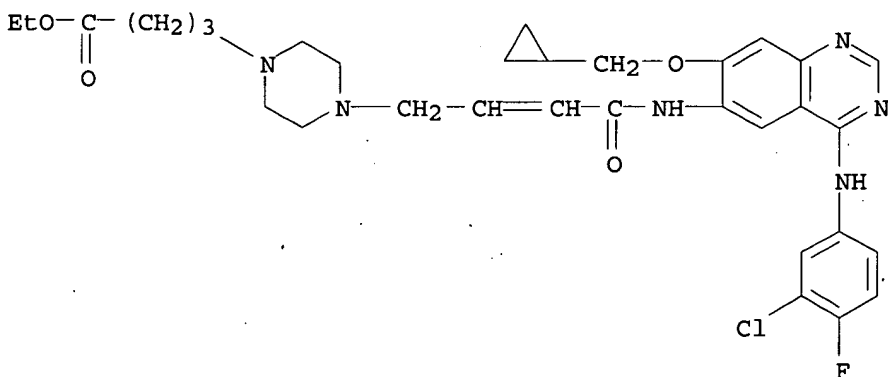
RN 290303-11-6 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-3-(ethoxycarbonyl)-, ethyl ester (9CI) (CA INDEX NAME)



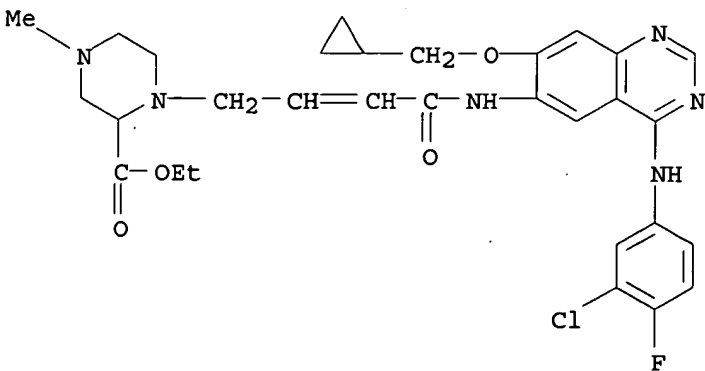
RN 290303-12-7 CAPLUS

CN 1-Piperazinebutanoic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290303-14-9 CAPLUS

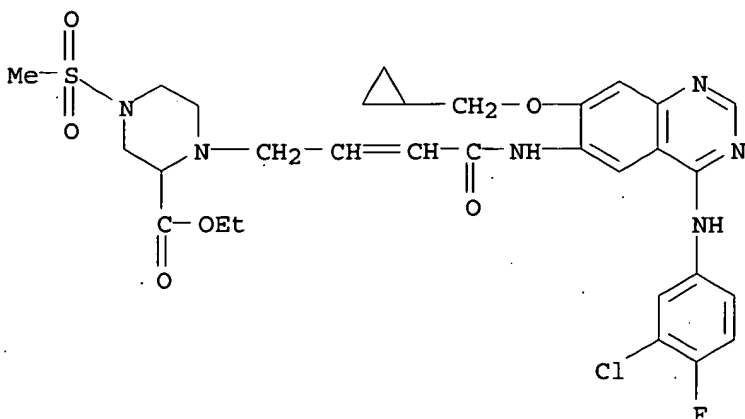
CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



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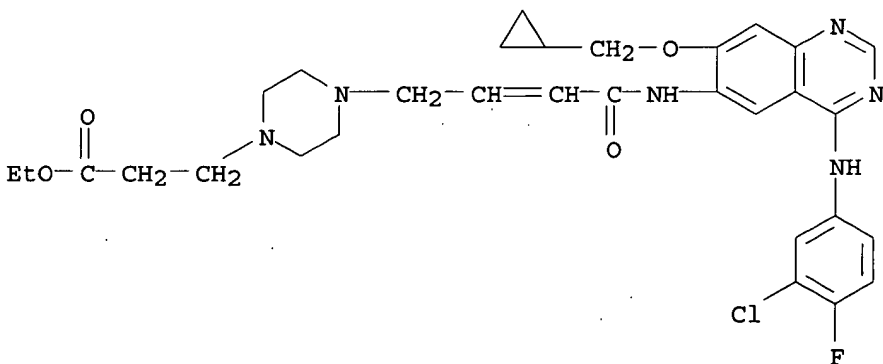
RN 290303-15-0 CAPLUS

CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-(methylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)



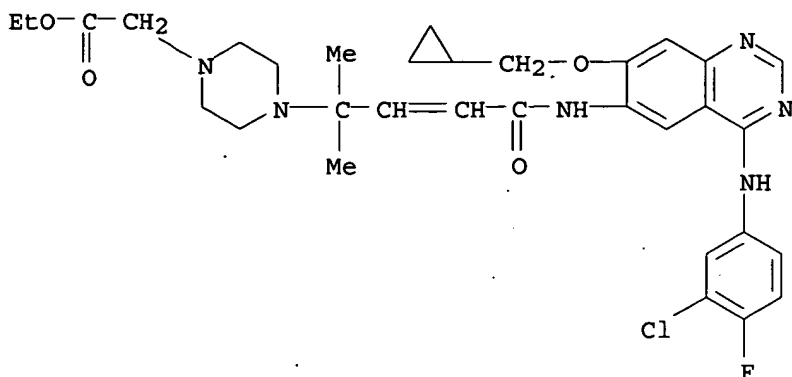
RN 290303-16-1 CAPLUS

CN 1-Piperazinepropanoic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



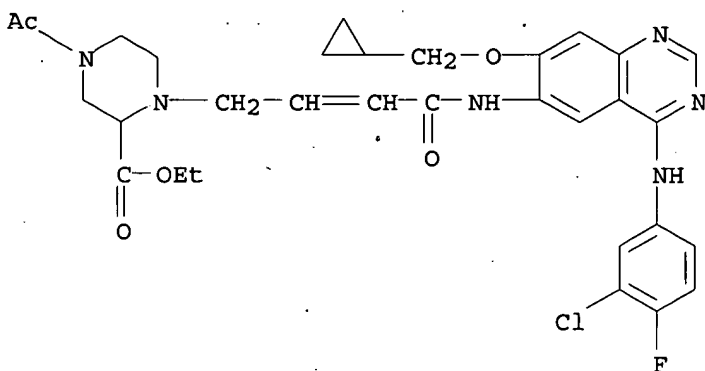
RN 290303-17-2 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,1-dimethyl-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290303-18-3 CAPLUS

CN 2-Piperazinecarboxylic acid, 4-acetyl-1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:607393 CAPLUS

DOCUMENT NUMBER: 133:207916

TITLE: Preparation of aminoquinazolines as epidermal growth factor receptor inhibitors.

INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K-G, Germany

SOURCE: Ger. Offen., 26 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

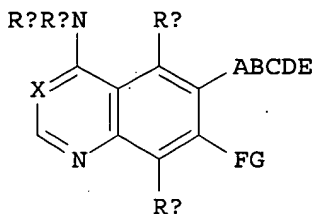
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908567	A1	20000831	DE 1999-19908567	19990227
CA 2361174	AA	20000908	CA 2000-2361174	20000224
WO 2000051991	A1	20000908	WO 2000-EP1496	20000224

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 NZ 513802 A 20010928 NZ 2000-513802 20000224
 EP 1157011 A1 20011128 EP 2000-910695 20000224
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 BR 2000008524 A 20011218 BR 2000-8524 20000224
 JP 2002538145 T2 20021112 JP 2000-602218 20000224
 EE 200100449 A 20021216 EE 2001-449 20000224
 BG 105765 A 20020329 BG 2001-105765 20010801
 HR 20010617 A1 20021031 HR 2001-617 20010823
 NO 2001004114 A 20011015 NO 2001-4114 20010824
 PRIORITY APPLN. INFO.: DE 1999-19908567 A 19990227
 DE 1999-19911366 A 19990315
 DE 1999-19928306 A 19990621
 US 1999-149329P P 19990817
 DE 1999-19954816 A 19991113
 WO 2000-EP1496 W 20000224

OTHER SOURCE(S): MARPAT 133:207916
 GI



AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH₂, 1-phenylethyl; Rc, Rm = H, F, Cl, MeO, (methoxy-, dimethylamino-, diethylamino-, pyrrolidino-, piperidino-, morpholino- substituted) Me; X = N, NCC; A = O, alkylimino; B = CO, SO₂; C = (Me- or F₃C-substituted) allenylene, vinylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, etc.; E, G = (substituted) R₆O₂CYNR₅, etc.; R₅ = H, (substituted) alkyl; R₆ = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl, etc.; F = alkylene, oxyalkylene, O; FG = H, F, Cl, alkoxy, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-[4-(ethoxycarbonyl)methylpiperazin-1-yl]propoxy]quinazoline (prepn. given) in CH₂Cl₂ contg. Et₃N was treated with acryloyl chloride in CH₂Cl₂ at -10.degree. to give 62% 4-[(3-bromophenyl)amino]-7-[3-[4-[(ethoxycarbonyl)methyl]piperazin-1-yl]propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation with IC₅₀ = 2.6 nM.

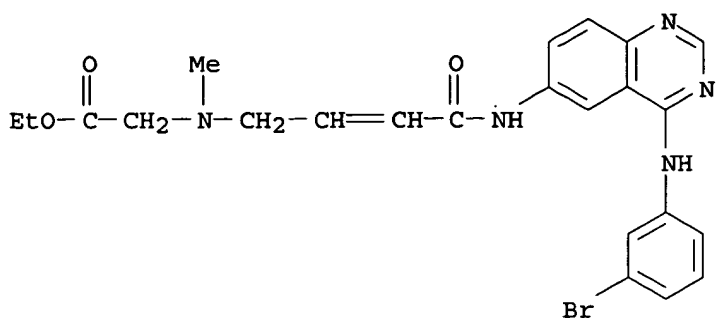
IT 289700-68-1P 289700-69-2P 289700-70-5P
 289700-71-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of aminoquinazolines as epidermal growth factor receptor inhibitors)

RN 289700-68-1 CAPLUS

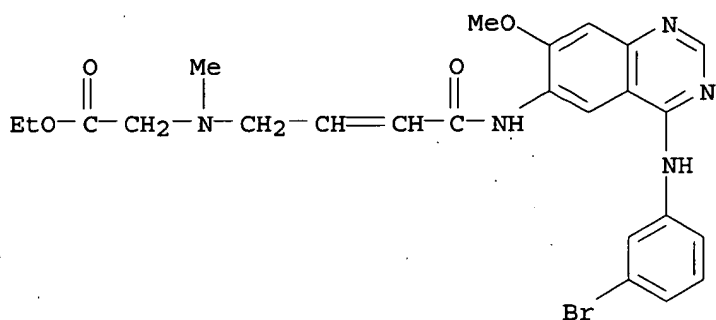
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

10/ 023,099



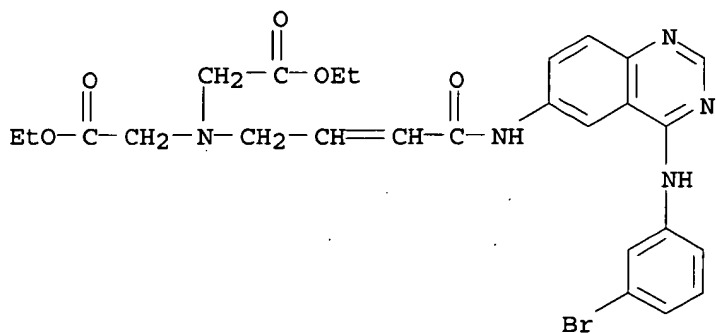
RN 289700-69-2 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



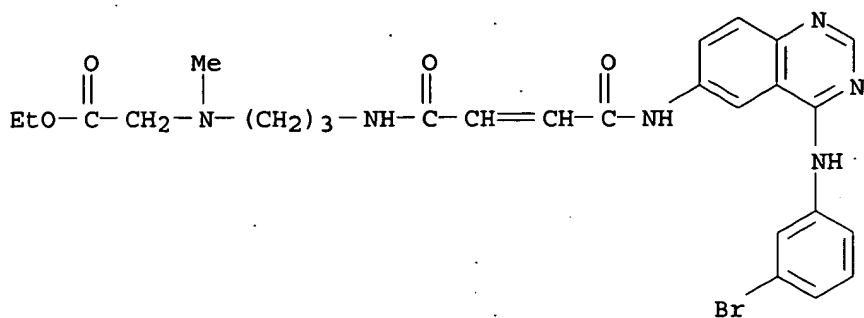
RN 289700-70-5 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-71-6 CAPLUS

CN Glycine, N-[3-[[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]amino]propyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:139833 CAPLUS

DOCUMENT NUMBER: 130:196664

TITLE: Preparation of 4-phenylaminoquinazolin-6-ylamides and related compounds as tyrosine kinase inhibitors.

INVENTOR(S): Wissner, Allan; Tsou, Hwei-ru; Johnson, Bernard Dean; Hamann, Philip Ross; Zhang, Nan

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 121 pp.

CODEN: PIXXD2

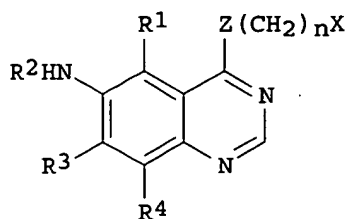
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909016	A1	19990225	WO 1998-US15789	19980729
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
TW 436485	B	20010528	TW 1998-87112356	19980728
AU 9886023	A1	19990308	AU 1998-86023	19980729
AU 757418	B2	20030220		
EP 1000039	A1	20000517	EP 1998-937275	19980729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9811805	A	20000815	BR 1998-11805	19980729
US 6251912	B1	20010626	US 1998-124365	19980729
JP 2001515071	T2	20010918	JP 2000-509699	19980729
ZA 9806905	A	20000131	ZA 1998-6905	19980731
NO 2000000487	A	20000331	NO 2000-487	20000131
PRIORITY APPLN. INFO.:				
			US 1997-904942	A 19970801
			US 1997-55072P	P 19970801
			WO 1998-US15789	W 19980729
OTHER SOURCE(S):		MARPAT 130:196664		
GI				



I

AB Title compds. [I; X = (substituted) cycloalkyl, pyridinyl, pyrimidinyl, Ph; Z = NH, O, S, NR; R = alkyl; R1, R3, R4 = H, halo, alkyl, alkenyl, alkynyl, alkenyloxy, alkynyloxy, CH2OH, halomethyl, alkanoyloxy, alkenoyloxy, alkynoyloxy, alkanoyloxymethyl, etc.; R2 = R5C.tplbond.CCO, (R5)2C:CR5CO, R5SS[C(R5)2]rCO, etc.; n = 0, 1; r = 1-4; R5 = H, CO2H, carboalkoxy, Ph, etc.], were prepd. Thus, 4-dimethylamino-2-butyric acid (prepn. given) was stirred with iso-Bu chloroformate and N-methylmorpholine in THF with ice cooling; N-(3-bromophenyl)-4,6-quinazolinediamine in pyridine was added and the mixt. was stirred 2 h at 0.degree. to give 4-dimethylamino-2-butyric acid [4-(3-bromophenylamino)quinazolin-6-yl]amide. The latter inhibited MB435 tumor cell growth with IC50 = 0.05 .mu.g/mL.

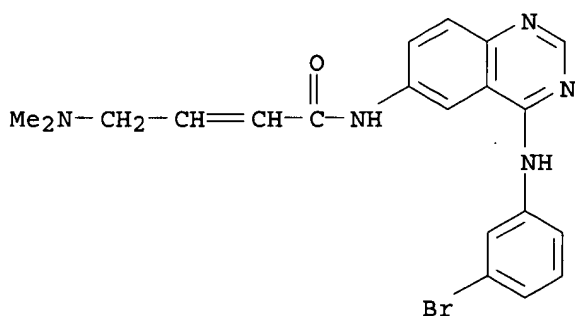
IT 220699-51-4P 220699-67-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 4-phenylaminoquinazolin-6-ylamides and related compds. as tyrosine kinase inhibitors)

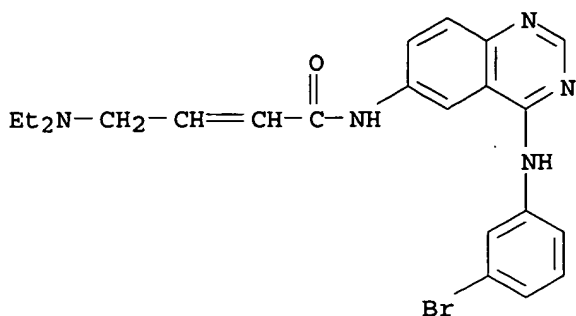
RN 220699-51-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 220699-67-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:113656 CAPLUS

DOCUMENT NUMBER: 130:168387

TITLE: Irreversible inhibitors of tyrosine kinases

INVENTOR(S): Bridges, Alexander James

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906378	A1	19990211	WO 1998-US15784	19980729
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9887607	A1	19990222	AU 1998-87607	19980729
US 6127374	A	20001003	US 1999-269545	19990325
US 6562818	B1	20030513	US 2000-593031	20000613
PRIORITY APPLN. INFO.: US 1997-54060P P 19970729				
WO 1998-US15784 W 19980729				
US 1999-269545 A3 19990325				

OTHER SOURCE(S): MARPAT 130:168387

AB Pyrimidine derivs. that are irreversible inhibitors of tyrosine kinases are reported. Thus, PhCH₂OH was treated with 4-FC₆H₄NO₂ to give 4-PhCH₂OC₆H₄NO₂, which was reduced to the amine and used to aminate 4-chloro-6-nitroquinazoline hydrochloride. The resulting 6-nitro-4-(4-benzyloxyanilino)quinazoline hydrochloride was reduced to the amine and acylated to give N-[4-(4-benzyloxyanilino)quinazolin-6-yl]acrylamide (I). I had an IC₅₀ for inhibition of epidermal growth factor receptor tyrosine kinase of 3.6 nM.

IT 220488-58-4P 220488-59-5P 220488-62-0P

220488-63-1P 220489-99-6P 220490-00-6P

220490-03-9P 220490-04-0P

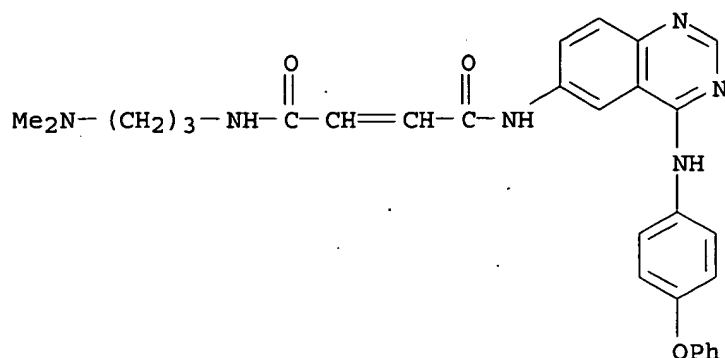
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of anilinoquinazolinylacrylamides and related compds. as tyrosine kinase inhibitors)

RN 220488-58-4 CAPLUS

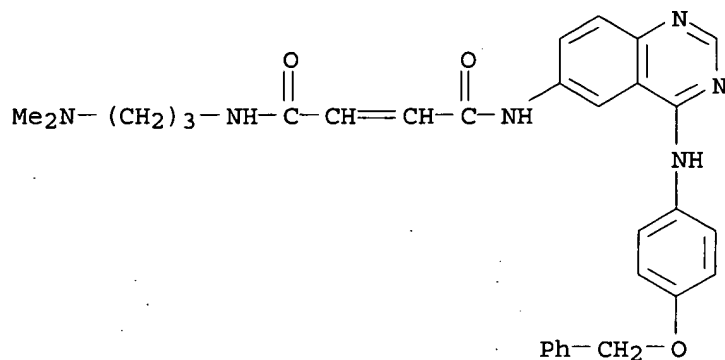
10/ 023,099

CN 2-Butenediamide, N-[3-(dimethylamino)propyl]-N'-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



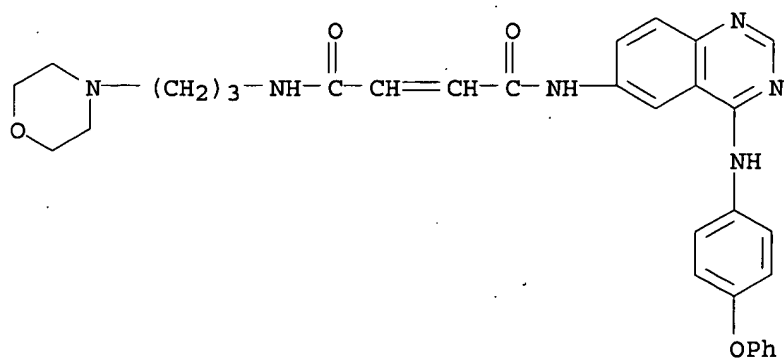
RN 220488-59-5 CAPLUS

CN 2-Butenediamide, N-[3-(dimethylamino)propyl]-N'-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 220488-62-0 CAPLUS

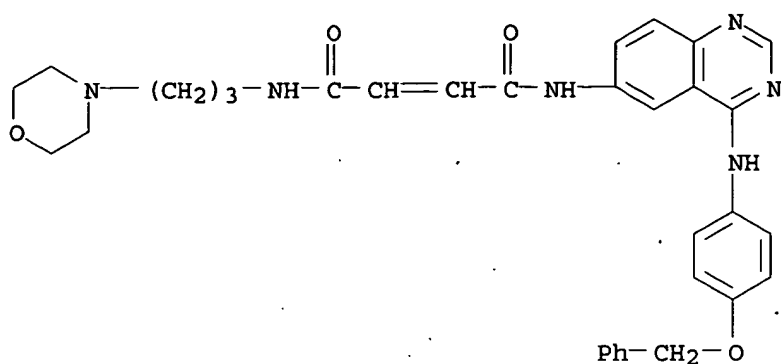
CN 2-Butenediamide, N-[3-(4-morpholinyl)propyl]-N'-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 220488-63-1 CAPLUS

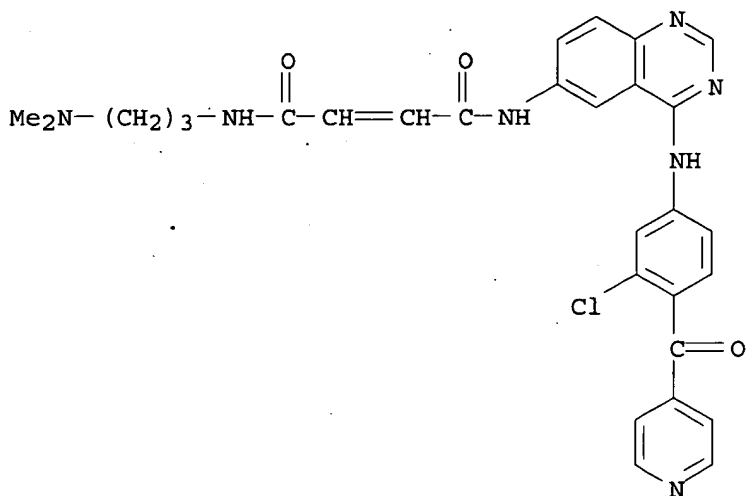
CN 2-Butenediamide, N-[3-(4-morpholinyl)propyl]-N'-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

10/ 023,099



RN 220489-99-6 CAPLUS

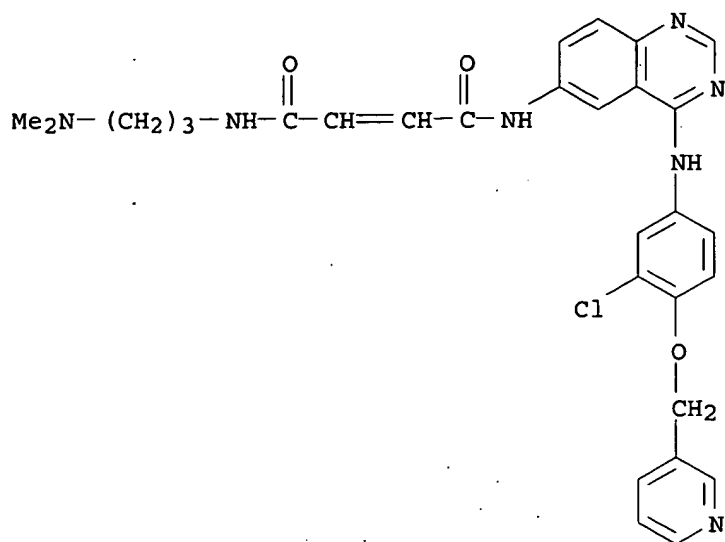
CN 2-Butenediamide, N-[4-[[3-chloro-4-(4-pyridinylcarbonyl)phenyl]amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



RN 220490-00-6 CAPLUS

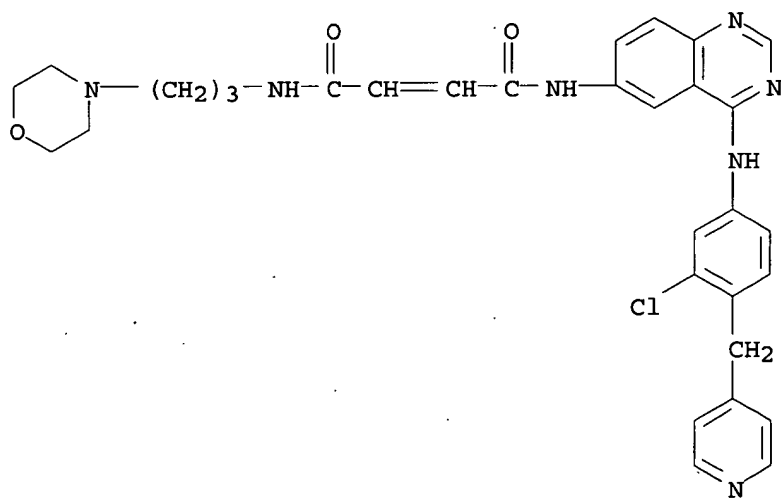
CN 2-Butenediamide, N-[4-[[3-chloro-4-(3-pyridinylmethoxy)phenyl]amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)

10/ 023,099



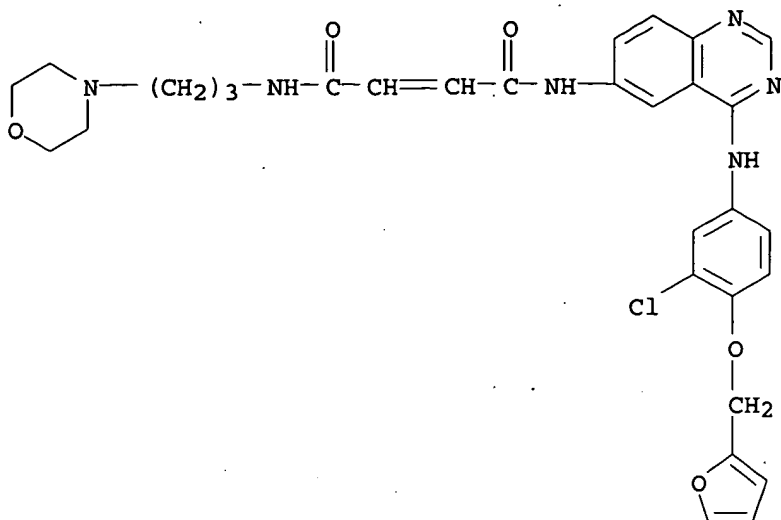
RN 220490-03-9 CAPLUS

CN 2-Butenediamide, N-[4-[[3-chloro-4-(4-pyridinylmethyl)phenyl]amino]-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl] - (9CI) (CA INDEX NAME)



RN 220490-04-0 CAPLUS

CN 2-Butenediamide, N-[4-[[3-chloro-4-(2-furanylmethoxy)phenyl]amino]-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl] - (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:696745 CAPLUS

DOCUMENT NUMBER: 128:3695

TITLE: Preparation of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors

INVENTOR(S): Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong; et al.

PATENT ASSIGNEE(S): Warner-Lambert Company, USA; Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong

SOURCE: PCT Int. Appl., 193 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

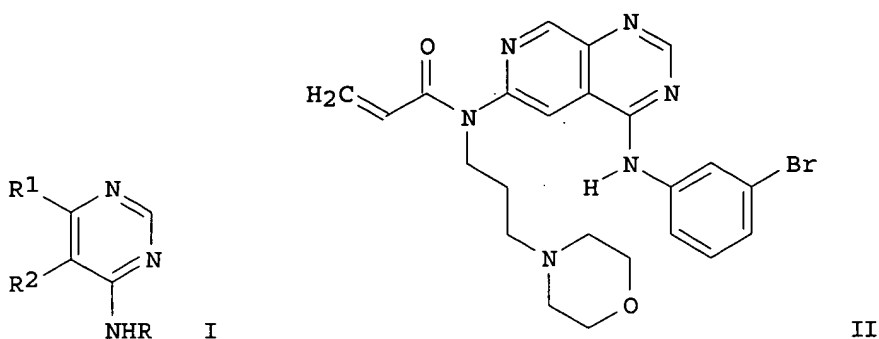
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9738983	A1	19971023	WO 1997-US5778	19970408
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AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:				
GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2249446	AA	19971023	CA 1997-2249446	19970408
AU 9724463	A1	19971107	AU 1997-24463	19970408
AU 725533	B2	20001012		
EP 892789	A1	19990127	EP 1997-920213	19970408
EP 892789	B1	20020227		
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				

10/ 023,099

CN 1218456	A	19990602	CN 1997-194458	19970408
BR 9708640	A	19990803	BR 1997-8640	19970408
JP 2000508657	T2	20000711	JP 1997-537173	19970408
JP 3370340	B2	20030127		
AT 213730	E	20020315	AT 1997-920213	19970408
ES 2174250	T3	20021101	ES 1997-920213	19970408
ZA 9703060	A	19971104	ZA 1997-3060	19970410
BG 63160	B1	20010531	BG 1998-102811	19981001
NO 9804718	A	19981209	NO 1998-4718	19981009
KR 2000005364	A	20000125	KR 1998-708086	19981010
US 6344459	B1	20020205	US 1999-155501	19990608
PRIORITY APPLN. INFO.:			US 1996-15351P	P 19960412
			WO 1997-US5778	W 19970408
OTHER SOURCE(S):		MARPAT 128:3695		
GI				



AB Title compds. [I; R = (CHR₆)pR₉; R₁R₂ = CH:CR₇CR₈:CH, CH:CR₇CR₈:N, CH:CR₇N:CH, etc.; R₆ = H or alkyl; 1 of R₇, R₈ = Z₁Z₂R₁₀ and the other = OR₄, SR₄, NHR₃; R₃, R₄ = (un)substituted alkyl, heterocyclalkyl, etc.; R₉ = (un)substituted Ph; R₁₀ = CR₁₁:CHR₅, C.tplbond.CR₅, CR₁₁:C:CHR₅; R₅ = H, halo, alkyl, Ph, etc.; R₁₁ = H, halo, alkyl; Z₁ = bond, O, (alkyl)imino, CH₂, etc.; Z₂ = CO, SO, P(O)(OH), etc.; p = 0 or 1] were prepd. Thus, I (R = C₆H₄Br-3, R₁R₂ = CH:NCR₈:CH, R₈ = F) was condensed with 3-morpholinopropylamine and the product acylated by CH₂:CHCOCl to give title compd. II. Data for biol. activity of I were given.

IT 198960-34-8P 198960-63-3P 198960-87-1P

198961-22-7P 198961-42-1P 198961-43-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors)

RN 198960-34-8 CAPLUS

CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]-, (2E)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

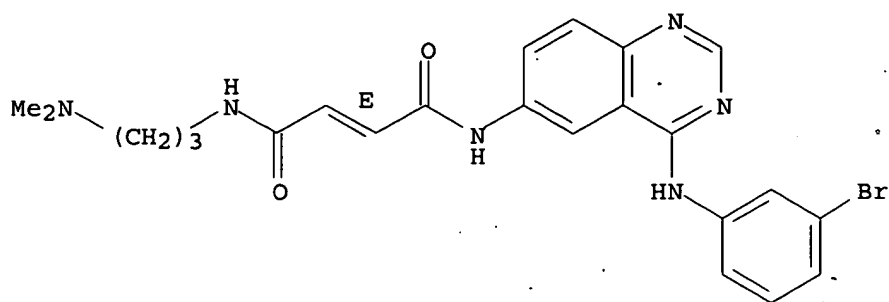
CM 1

CRN 198960-33-7

CMF C23 H25 Br N6 O2

Double bond geometry as shown.

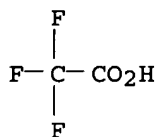
10/ 023,099



CM 2

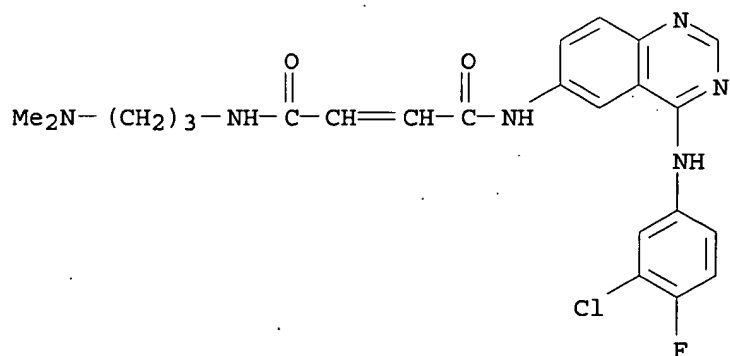
CRN 76-05-1

CMF C2 H F3 O2



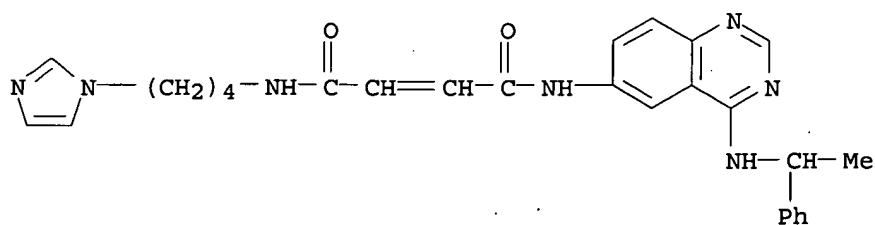
RN 198960-63-3 CAPLUS

CN 2-Butenediamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



RN 198960-87-1 CAPLUS

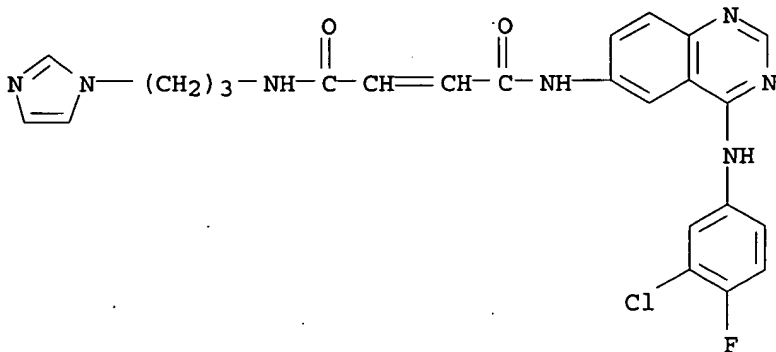
CN 2-Butenediamide, N-[4-(1H-imidazol-1-yl)butyl]-N'-[4-[(1-phenylethyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



10/ 023,099

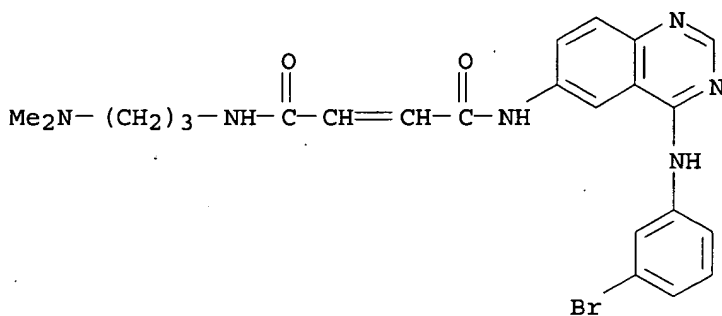
RN 198961-22-7 CAPLUS

CN 2-Butenediamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N'-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



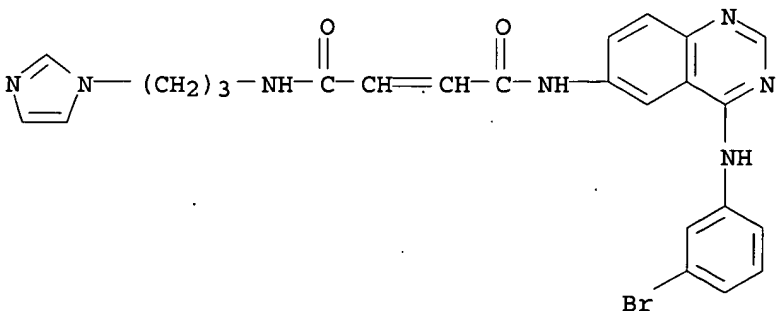
RN 198961-42-1 CAPLUS

CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



RN 198961-43-2 CAPLUS

CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



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10/ 023,099

L1 STRUCTURE UPLOADED
L2 306 S L1 FUL

. FILE 'CAPLUS' ENTERED AT 13:07:58 ON 01 JUL 2003
L3 13 S L2

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

60.64

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

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CA SUBSCRIBER PRICE

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-8.46

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